

DOCUMENTA GEIGY
SCIENTIFIC TABLES • SEVENTH EDITION

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'Pathogenic Organisms and Infectious Diseases' (in preparation)

DOCUMENTA
GEIGY

SCIENTIFIC TABLES

SEVENTH EDITION

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Publisher's Foreword

This 7th edition of the *Geigy Scientific Tables* pursues the aim of earlier editions, namely to provide doctors and biologists with basic data in a concise form and thus spare them much searching in the literature.

In the 6th edition the main changes from the previous edition consisted of an extension of the mathematical, physical and chemical data and a new chapter devoted to biochemistry; in this edition the principal difference is the greatly expanded medical part of the book. The increasing extent to which physical, physicochemical and biochemical methods are finding application in medicine has resulted in the last few years in an immense accumulation of new data whose proper evaluation can be undertaken only by specialists. For this reason we have been compelled in this edi-

tion to enlist the cooperation of outside experts to a much greater degree than in the past. Here we would like to thank all those who have contributed in this way – whether in the form of original article or expert advice – for their invaluable help. Their names are listed overleaf.

We would also like to express our appreciation once again of the assistance of all those who have made suggestions or drawn our attention to errors. If we have been unable to adopt all the suggestions put to us, this has been due to the limits set us by the physical compass of the *Scientific Tables*. Users can rest assured that we shall continue to do our best to meet their wishes in the future.

J.R.GEIGY S.A., Basle

Editors' Foreword

All the fields covered by the 6th edition of the *Scientific Tables* are again represented in this new edition with the exception of 'Infectious Diseases', the chapter on which appears separately as a supplement. The thoroughgoing revision of the remaining chapters has resulted in a number of major changes, of which the following are worthy of special mention

The data on units of measurement and the physical constants take account of decisions and recommendations adopted by the various international commissions up to March 1969, in particular those concerned with the introduction of the International System of Units. The adoption of the unified scale of atomic weights based on the isotope carbon-12 has involved the recalculation of molecular weights throughout the book. In the physicochemical part of the book a chapter on pH standards has been added, and the data on buffer solutions have been recalculated to the pH scale of the National Bureau of Standards.

'Biochemistry' has been greatly enlarged, particularly by the inclusion of more data on nucleic acids and protein and fatty-acid synthesis as well as by the addition of a new chapter on 'Inborn Errors of Metabolism'. Throughout this section – as in the other sections – the recommendations on nomenclature made by the International Union of Pure and

Applied Chemistry and the International Union of Biochemistry have been largely adhered to.

In the section on nutrition due regard has been paid to the considerable advances made in recent years in knowledge of the nutritional significance of the vitamins; and important new sources have been utilized in revising the data on the composition of foods.

Of the chapters comprising the section on 'Composition and Functions of the Body', those on the composition of the body, renal function and respiration in particular have been greatly extended. Under the heading of 'body fluids' the subject of blood enzymes has been given much more thorough treatment, and chapters on the synovial fluid and sweat have been added.

Under body measurements the normal data of pregnancy have been completely revised, and the chapter now includes tables of weights of the organs.

The final section of the book is now that on hormones, an arrangement that has permitted the inclusion of more recent endocrinological data from this rapidly advancing field than would otherwise have been possible.

K. DIEM
C. LENTNER

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Contents

Mathematics and statistics

Constants	9
Logarithms	10
Reciprocals, powers and roots	18
Binomial coefficients	25
Factorials	26
Statistical tables	28
Mathematical symbols, definitions and formulae	132
Statistical methods	
Contents	145
Introduction	146
Index	197

Physics

Symbols of units.	199
Mechanical and thermal units.	200
Electrical and magnetic units.	215
Radioactivity and radiation dosimetry.	217
Electromagnetic radiation and light units.	222
Acoustical units.	224
Unit of amount of substance.	226
Physical constants.	228

Physical chemistry

Elements	
Periodic system.	231
Alphabetical tables.	232
Properties, abundance, isotopes.	234
Electronic configurations.	240
Multiples of atomic weights.	250
Chemical conversion factors.	251
ICAO normal atmosphere.	252
Mercury barometer correction.	255
Saturation pressure of water vapour.	256
Vapour pressure and boiling point of water.	257
Reduction of gas volumes.	259
Aqueous solutions	
Introduction.	270
Calculation of freezing point depression and osmotic pressure.	272
Calculation of salt and glucose concentrations.	273
Conversion factors for electrolytes.	274
Deionormal solutions.	277
pH standards.	278
Buffer solutions.	280
Acid-base indicators.	283
Flame photometry lines.	284
Radioactive nuclides	
Principles.	285
Diagnostic uses.	287
Therapeutic uses.	290
Characteristics.	292
Decay tables.	294
Biochemistry	
Contents.	307
Constituents of living matter.	308
Metabolism.	387
Inborn errors of metabolism.	446
Nutrition	
Vitamins	
Vitamin A.	457

Vitamin D.	461
Vitamin E.	464
Vitamin K.	467
Thiamine.	469
Riboflavin.	471
Vitamin B ₆	473
Nicotinic acid.	476
Folic acid group.	478
Vitamin B ₁₂ group.	482
Biotin.	486
Pantothenic acid.	487
Ascorbic acid.	489
Vitaminoids.	491
Nutritional standards.	493
Foods	
Principal nutrients and minerals.	498
Amino acids.	516
Composition and functions of the body	
Chemical composition of the body.	517
Water and electrolyte balance.	523
Renal function values.	531
Body surface area.	537
Basal metabolism.	539
Respiration.	541
Blood pressure.	553
Blood volume.	554
Body fluids	
Blood	
Physicochemical data.	557
Inorganic substances.	561
Blood gases.	568
Nitrogenous substances.	572
Proteins.	579
Enzymes.	584
Lipids.	600
Carbohydrates.	604
Non-nitrogenous metabolites.	606
Vitamins.	609
Blood cells	
Erythroblasts.	612
Reticulocytes.	612
Erythrocytes.	613
Leucocytes.	618
Thrombocytes.	620
Bone marrow.	621
Blood coagulation.	622
Blood groups.	626
Serum groups.	634
Cerebrospinal fluid.	635
Synovial fluid.	640
Saliva.	643
Gastric juice.	647
Pancreatic juice.	651
Bile.	653
Intestinal juice.	656
Faeces.	657
Urine	
Physicochemical data.	661
Inorganic substances.	662
Nitrogenous substances.	665

Contents

Enzymes.....	672	Oxytocin and vasopressin.....	722
Carbohydrates.....	673	Hypothalamic pituitary-regulating factors.....	725
Non-nitrogenous metabolites.....	674	Thyroid hormones.....	725
Vitamins.....	676	Parathyroid hormone.....	728
Sediments.....	677	Calcitonin.....	729
Sweat.....	679	Thymus hormone.....	730
Semen.....	682	Hormones of the pineal gland.....	730
Spermatozoa.....	686	Catecholamines.....	730
Breast milk.....	687	Insulin.....	734
		Glucagon.....	737
Body measurements		Hormones of the gastrointestinal tract.....	739
Pregnancy.....	690	Erythropoietin.....	740
Normal measurements during growth.....	692	Renin-angiotensin system.....	740
Appearance of secondary ossification centres.....	706	Plasma kinins.....	742
Development of the teeth.....	709	Corticosteroids.....	742
Weights of the organs.....	710	Androgens.....	751
Average and desirable weights of adults.....	711	Progesterone.....	753
		Oestrogens.....	755
Hormones		Function of the sex hormones.....	758
Gonadotropins of the anterior pituitary.....	713	International biological standards and reference preparations.....	759
Chorionic gonadotropin.....	715		
Corticotropin.....	716	Index	765
Thyrotropin.....	718		
Prolactin.....	718	Addenda and errata	809
Growth hormone.....	719		
Placental lactogen.....	721	Folia medica Geigy	(inside back cover)
Melanotropin.....	721		

Notes for the guidance of users

Apart from the main contents (above) and general index (pages 765 et seq.) the user will find the contents of the chapter on 'Statistical Methods' on page 145, that of the chapters on 'Constituents of Living Matter' and 'Metabolism' on page 307; in addition there is a separate detailed index to the chapter on 'Statistical Methods' on pages 197-198.

Zero values are indicated by the figure 0 throughout the book. A dash (-) signifies that the value is unknown, and this sign should on no account be interpreted as a zero value.

As a rule, the meanings of symbols and abbreviations are given where they first occur. For units of measurement an alphabetical list is available on page 199.

In the numerical tables, a point over the last figure (or figures) indicates a recurring figure (or figures), thus

$$1.\dot{6} = 1.666666\dots$$

$$1.652\dot{7}8 = 1.65278278278\dots$$

In general the number of places given has been dictated by the space available. The user should abstract as many as he needs and round off accordingly.

Exact values have been distinguished from rounded-off values by printing the last figure in bold-face type. Thus, 1.1257 would be the rounded-off value of, say, 1.1257354..., while 1.1257 is an exact number. This notation is used in particular for the arbitrarily defined values of constants.

When they have been calculated according to statistical procedures (usually as mean value ± 2 standard deviations), normal ranges are given under the heading '95% range' (note that this practice differs from that adopted in previous editions).

For obvious reasons we have had to restrict bibliographical references to a representative selection of recently published original papers and reviews. In fields where research activity is currently high a rather fuller bibliography is given. The abbreviations used in the literature references are those recommended by the UNESCO and WHO (*World Medical Periodicals*, World Medical Association, New York, 1961).

Additional copies of the *Folia medica Geigy* in the inside back cover of this book may be obtained by application to J.R. Geigy S.A., CH-4000 Basle 18, Switzerland.

Mathematical constants

Bernoulli numbers		Euler numbers		Prime numbers < 100	
n	B_n	n	E_n	Number	\log_{10} (mantissa)
1	1/6	1	1	2	30102 99956 63981 19521
2	1/30	2	5	3	47712 12547 19662 43730
3	1/42	3	61	5	69897 00043 36018 80479
4	1/30	4	1385	7	84509 80400 14256 83071
5	5/66	5	50521	11	04139 26851 58225 04075
6	691/2730	6	2702765	13	11394 33523 06836 76921
7	7/6	7	1993 60981	17	23044 89213 78273 92854
8	3617/510	8	193915 12145	19	27875 36009 52828 96154
9	43867/798	9	240 48796 75441	23	36172 78360 17592 87887
10	174611/330	10	37037 11882 37525	29	46239 79978 98956 08733
11	8 54513/138	11	69 34887 43931 37901	31	49136 16938 34272 67967
12	2363 64091/2730	12	15514 53416 35570 86905	37	56820 17240 66994 99681
13	85 53103/6	13	40 87072 50929 31238 92361	41	61278 38567 19735 49451
Primes					
Constants					
Constant	Value	\log_{10}			
π	3 14159 26535 89793 23846	0 49714 98726 94133 85435	43	63346 84555 79586 52641	
π^2	9 86960 44010 89358 61883	0 99429 97453 88267 70870	47	67209 78579 35717 46441	
$(2\pi)^{-1/2}$	0 39894 22804 01432 67794	0 60091 00658 20942 47522-1	53	72427 58696 00789 04563	
e	2.71828 18284 59045 23536	= M	59	77085 20116 42144 19026	
$M = \log_{10} e = \lg e$	0 43429 44819 03251 82765		61	78532 98350 10767 03389	
$1/M = \log_e 10 = \ln 10$	2 30258 50929 94045 68402	0 76133 81087 83167 61054-1	67	82607 48027 00826 43415	
γ (Euler's constant)	0 57721 56649 01532 86061		71	85125 83487 19075 28609	
			73	86332 28601 20455 90107	
			79	89762 70912 90441 42799	
			83	91907 80925 76073 90383	
			89	94939 00066 44912 78472	
			97	98677 17342 66244 85178	

Greek alphabet

Greek character		Greek name	Roman equivalent
A α	Α α	alpha	A a
B β	Β β	beta	B b
Γ γ	Γ γ	gamma	G g
Δ δ	Δ δ	delta	D d
E ε, ε	Ε ε, ε	epsilon	Ε ε
Z ζ	Ζ ζ	zeta	Z z
H η	Η η	eta	E ē
Θ θ, θ	Θ θ, θ	theta	Th th
I ι	Ι ι	iota	I i
K κ, κ	Κ κ, κ	kappa	K k
Λ λ	Λ λ	lambda	L l
M μ	Μ μ	mu	M m
N ν	Ν ν	nu	N n
Ξ ξ	Ξ ξ	xi	X x
O ο	Ο ο	omicron	Ö ö
Π π, π	Π π, π	pi	P p
Ρ ρ	Ρ ρ	rho	R r
Σ σ, σ	Σ σ, σ	sigma	S s
T τ	Τ τ	tau	T t
Υ υ	Υ υ	upsilon	Y y
Φ φ, φ	Φ φ, φ	phi	Ph ph
Χ χ	Χ χ	chi	Ch ch
Ψ ψ	Ψ ψ	psi	Psi ps
Ω ω	Ω ω	omega	Ū ū

Prefixes and symbols for decimal multiples and submultiples of units¹

Power of ten	Prefix	Symbol
10 ¹²	tera	T
10 ⁹	giga	G
10 ⁶	mega	M
10 ³	kilo	k
10 ²	hecto	h
10 ¹	deca*	da
10 ⁻¹	deci	d
10 ⁻²	centi	c
10 ⁻³	milli	m
10 ⁻⁶	micro	μ
10 ⁻⁹	nano	n
10 ⁻¹²	pico	p
10 ⁻¹⁵	femto	f
10 ⁻¹⁸	atto	a

* Also 'deka'.

Four-Place Common Logarithms

N	log x										Proportional parts							
	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8
100	0000	0004	0009	0013	0017	0022	0026	0030	0035	0039	0	1	1	2	2	3	3	3
101	0043	0048	0052	0056	0060	0065	0069	0073	0077	0082	0	1	1	2	2	3	3	3
102	0086	0090	0095	0099	0103	0107	0111	0116	0120	0124	0	1	1	2	2	3	3	3
103	0128	0133	0137	0141	0145	0149	0154	0158	0162	0166	0	1	1	2	2	3	3	3
104	0170	0175	0179	0183	0187	0191	0195	0199	0204	0208	0	1	1	2	2	3	3	3
105	0212	0216	0220	0224	0228	0233	0237	0241	0245	0249	0	1	1	2	2	3	3	3
106	0253	0257	0261	0265	0269	0273	0278	0282	0286	0290	0	1	1	2	2	3	3	3
107	0294	0298	0302	0306	0310	0314	0318	0322	0326	0330	0	1	1	2	2	3	3	3
108	0334	0338	0342	0346	0350	0354	0358	0362	0366	0370	0	1	1	2	2	3	3	3
109	0374	0378	0382	0386	0390	0394	0398	0402	0406	0410	0	1	1	2	2	3	3	3
10	0000	0043	0086	0128	0170	0212	0253	0294	0334	0374	4	8	12	17	21	25	29	33
11	0414	0453	0492	0531	0569	0607	0645	0682	0719	0755	4	8	11	15	19	23	26	30
12	0792	0828	0864	0899	0934	0969	1004	1038	1072	1106	3	7	10	14	17	21	24	28
13	1139	1173	1206	1239	1271	1303	1335	1367	1399	1430	3	6	10	13	16	19	23	26
14	1461	1492	1523	1553	1584	1614	1644	1673	1703	1732	3	6	9	12	15	18	21	24
15	1761	1790	1818	1847	1875	1903	1931	1959	1987	2014	3	6	8	11	14	17	20	22
16	2041	2068	2095	2122	2148	2175	2201	2227	2253	2279	3	5	8	11	13	16	18	21
17	2304	2330	2355	2380	2405	2430	2455	2480	2504	2529	2	5	7	10	12	15	17	20
18	2553	2577	2601	2625	2648	2672	2695	2718	2742	2765	2	5	7	9	12	14	16	19
19	2788	2810	2833	2856	2878	2900	2923	2945	2967	2989	2	4	7	9	11	13	16	18
20	3010	3032	3054	3075	3096	3118	3139	3160	3181	3201	2	4	6	8	11	13	15	17
21	3222	3243	3263	3284	3304	3324	3345	3365	3385	3404	2	4	6	8	10	12	14	16
22	3424	3444	3464	3483	3502	3522	3541	3560	3579	3598	2	4	6	8	10	12	14	15
23	3617	3636	3655	3674	3692	3711	3729	3747	3766	3784	2	4	6	7	9	11	13	15
24	3802	3820	3838	3856	3874	3892	3909	3927	3945	3962	2	4	5	7	9	11	12	14
25	3979	3997	4014	4031	4048	4065	4082	4099	4116	4133	2	3	5	7	9	10	12	14
26	4150	4166	4183	4200	4216	4232	4249	4265	4281	4298	2	3	5	7	8	10	11	13
27	4314	4330	4346	4362	4378	4393	4409	4425	4440	4456	2	3	5	6	8	9	11	13
28	4472	4487	4502	4518	4533	4548	4564	4579	4594	4609	2	3	5	6	8	9	11	12
29	4624	4639	4654	4669	4683	4698	4713	4728	4742	4757	1	3	4	6	7	9	10	12
30	4771	4786	4800	4814	4829	4843	4857	4871	4886	4900	1	3	4	6	7	9	10	11
31	4914	4928	4942	4955	4969	4983	4997	5011	5024	5038	1	3	4	6	7	8	10	11
32	5051	5065	5079	5092	5105	5119	5132	5145	5159	5172	1	3	4	5	7	8	9	11
33	5185	5198	5211	5224	5237	5250	5263	5276	5289	5302	1	3	4	5	6	8	9	10
34	5315	5328	5341	5353	5366	5378	5391	5403	5416	5428	1	3	4	5	6	8	9	10
35	5441	5453	5465	5478	5490	5502	5514	5527	5539	5551	1	2	4	5	6	7	9	10
36	5563	5575	5587	5599	5611	5623	5635	5647	5658	5670	1	2	4	5	6	7	8	10
37	5682	5694	5705	5717	5729	5740	5752	5763	5775	5786	1	2	3	5	6	7	8	9
38	5798	5809	5821	5832	5843	5855	5866	5877	5888	5899	1	2	3	4	5	6	7	8
39	5911	5922	5933	5944	5955	5966	5977	5988	5999	6010	1	2	3	4	5	6	7	8
40	6021	6031	6042	6053	6064	6075	6085	6096	6107	6117	1	2	3	4	5	6	8	9
41	6128	6138	6149	6160	6170	6180	6191	6201	6212	6222	1	2	3	4	5	6	7	8
42	6232	6243	6253	6263	6274	6284	6294	6304	6314	6325	1	2	3	4	5	6	7	8
43	6335	6345	6355	6365	6375	6385	6395	6405	6415	6425	1	2	3	4	5	6	7	8
44	6435	6444	6454	6464	6474	6484	6493	6503	6513	6522	1	2	3	4	5	6	7	8
45	6532	6542	6551	6561	6571	6580	6590	6599	6609	6618	1	2	3	4	5	6	7	8
46	6628	6637	6646	6656	6665	6675	6684	6693	6702	6712	1	2	3	4	5	6	7	7
47	6721	6730	6739	6749	6758	6767	6776	6785	6794	6803	1	2	3	4	5	6	7	7
48	6812	6821	6830	6839	6848	6857	6866	6875	6884	6893	1	2	3	4	4	5	6	7
49	6902	6911	6920	6928	6937	6946	6955	6964	6972	6981	1	2	3	4	4	5	6	7
50	6990	6998	7007	7016	7024	7033	7042	7050	7059	7067	1	2	3	3	4	5	6	7
51	7076	7084	7093	7101	7110	7118	7126	7135	7143	7152	1	2	3	3	4	5	6	7
52	7160	7168	7177	7185	7193	7202	7210	7218	7226	7235	1	2	2	3	4	5	6	7
53	7243	7251	7259	7267	7275	7284	7292	7300	7308	7316	1	2	2	3	4	5	6	6
54	7324	7332	7340	7348	7356	7364	7372	7380	7388	7396	1	2	2	3	4	5	6	6
55	7404	7412	7419	7427	7435	7443	7451	7459	7466	7474	1	2	2	3	4	5	5	6
56	7482	7490	7497	7505	7513	7520	7528	7536	7543	7551	1	2	2	3	4	5	5	6
57	7559	7566	7574	7582	7589	7597	7604	7612	7619	7627	1	2	2	3	4	5	5	6
58	7634	7642	7649	7657	7664	7672	7679	7686	7694	7701	1	1	2	3	4	4	5	6
59	7709	7716	7723	7731	7738	7745	7752	7760	7767	7774	1	1	2	3	4	4	5	6
60	7782	7789	7796	7803	7810	7818	7825	7832	7839	7846	1	1	2	3	4	4	5	6
61	7853	7860	7868	7875	7882	7889	7896	7903	7910	7917	1	1	2	3	4	4	5	6
62	7924	7931	7938	7945	7952	7959	7966	7973	7980	7987	1	1	2	3	4	4	5	6
63	7993	8000	8007	8014	8021	8028	8035	8041	8048	8055	1	1	2	3	4	4	5	6
64	8062	8069	8075	8082	8089	8096	8102	8109	8116	8122	1	1	2	3	4	4	5	6
65	8129	8136	8142	8149	8156	8162	8169	8176	8182	8189	1	1	2	3	4	4	5	6
66	8195	8202	8209	8215	8222	8228	8235	8241	8248	8254	1	1	2	3	4	4	5	6
67	8261	8267	8274	8280	8287	8293	8299	8306	8312	8319	1	1	2	3	4	4	5	6
68	8325	8331	8338	8344	8351	8357	8363	8370	8376	8382	1	1	2	3	4	4	5	6
69	8388	8395	8401	8407	8414	8420	8426	8432	8439	8445	1	1	2	2	3	4	4	5
70	8451	8457	8463	8470	8476	8482	8488	8494	8500	8506	1	1	2	2	3	4	4	5
71	8513	8519	8525	8531	8537	8543	8549	8555	8561	8567	1	1	2	2	3	4	4	5
72	8573	8579	8585	8591	8597	8603	8609	8615	8621	8627	1	1	2	2	3	4	4	5
73	8633	8639	8645	8651	8657	8663	8669	8675	8681	8686	1	1	2	2	3	4	4	5
74	8692	8698	8704	8710	8716	8722	8727	8733	8739	8745	1	1	2	2	3	4	4	5
75	8751	8756	8762	8768	8774	8779	8785	8791	8797	8802	1	1	2	2	3	4	4	5
76	8808	8814	8820	8825	8831	8837	8842	8848	8854	8859	1	1	2	2	3	4	4	5
77	8865	8871	8876	8882	8887	8893	8899	8904	8910	8915	1	1	2	2	3	4	4	5
78	8921	8927	8932	8938	8943	8949	8954	8960	8965	8971	1	1	2	2	3	4	4	5
79	8976	8982																

log x	x										Proportional parts									
	0	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9	
.00	1000	1002	1005	1007	1009	1012	1014	1016	1019	1021	0	0	1	1	1	1	1	1	1	
.01	1023	1026	1028	1030	1033	1035	1038	1040	1042	1045	0	0	1	1	1	1	1	1	1	
.02	1047	1050	1052	1054	1057	1059	1062	1064	1067	1069	0	0	1	1	1	1	1	1	1	
.03	1072	1074	1076	1079	1081	1084	1086	1089	1091	1094	0	0	1	1	1	1	1	1	1	
.04	1096	1099	1102	1104	1107	1109	1112	1114	1117	1119	0	0	1	1	1	1	1	1	1	
.05	1122	1125	1127	1130	1132	1135	1138	1140	1143	1146	0	0	1	1	1	1	1	1	1	
.06	1148	1151	1153	1156	1159	1161	1164	1167	1169	1172	0	0	1	1	1	1	1	1	1	
.07	1175	1178	1180	1183	1186	1189	1191	1194	1197	1199	0	0	1	1	1	1	1	1	1	
.08	1202	1205	1208	1211	1213	1216	1219	1222	1225	1227	0	0	1	1	1	1	1	1	1	
.09	1230	1233	1236	1239	1242	1245	1247	1250	1253	1256	0	0	1	1	1	1	1	1	1	
.10	1259	1262	1265	1268	1271	1274	1276	1279	1282	1285	0	0	1	1	1	1	1	1	1	
.11	1288	1291	1294	1297	1300	1303	1306	1309	1312	1315	0	0	1	1	1	1	1	1	1	
.12	1318	1321	1324	1327	1330	1334	1337	1340	1343	1346	0	0	1	1	1	1	1	1	1	
.13	1349	1352	1355	1358	1361	1365	1368	1371	1374	1377	0	0	1	1	1	1	1	1	1	
.14	1380	1384	1387	1390	1393	1396	1400	1403	1406	1409	0	0	1	1	1	1	1	1	1	
.15	1413	1416	1419	1422	1426	1429	1432	1435	1439	1442	0	0	1	1	1	1	1	1	1	
.16	1445	1449	1452	1455	1459	1462	1466	1469	1472	1476	0	0	1	1	1	1	1	1	1	
.17	1479	1483	1486	1489	1493	1496	1500	1503	1507	1510	0	0	1	1	1	1	1	1	1	
.18	1514	1517	1521	1524	1528	1531	1535	1538	1542	1545	0	0	1	1	1	1	1	1	1	
.19	1549	1552	1556	1560	1563	1567	1570	1574	1578	1581	0	0	1	1	1	1	1	1	1	
.20	1585	1589	1592	1596	1600	1603	1607	1611	1614	1618	0	0	1	1	1	1	1	1	1	
.21	1622	1626	1629	1633	1637	1641	1644	1648	1652	1656	0	0	1	1	1	1	1	1	1	
.22	1660	1663	1667	1671	1675	1679	1683	1687	1690	1694	0	0	1	1	1	1	1	1	1	
.23	1698	1702	1706	1710	1714	1718	1722	1726	1730	1734	0	0	1	1	1	1	1	1	1	
.24	1738	1742	1746	1750	1754	1758	1762	1766	1770	1774	0	0	1	1	1	1	1	1	1	
.25	1778	1782	1786	1791	1795	1799	1803	1807	1811	1815	0	0	1	1	1	1	1	1	1	
.26	1820	1824	1828	1832	1837	1841	1845	1849	1853	1858	0	0	1	1	1	1	1	1	1	
.27	1862	1867	1871	1875	1879	1884	1888	1892	1896	1900	0	0	1	1	1	1	1	1	1	
.28	1905	1910	1914	1919	1923	1928	1932	1936	1941	1945	0	0	1	1	1	1	1	1	1	
.29	1950	1954	1959	1963	1968	1972	1977	1982	1986	1991	0	0	1	1	1	1	1	1	1	
.30	1995	2000	2004	2009	2014	2018	2023	2028	2032	2037	0	0	1	1	1	1	1	1	1	
.31	2042	2046	2051	2056	2061	2065	2070	2075	2080	2084	0	0	1	1	1	1	1	1	1	
.32	2089	2094	2099	2104	2109	2113	2118	2123	2128	2133	0	0	1	1	1	1	1	1	1	
.33	2138	2143	2148	2153	2158	2163	2168	2173	2178	2183	0	0	1	1	1	1	1	1	1	
.34	2188	2193	2198	2203	2208	2213	2218	2223	2228	2234	0	0	1	1	1	1	1	1	1	
.35	2239	2244	2249	2254	2259	2265	2270	2275	2280	2286	0	0	1	1	1	1	1	1	1	
.36	2291	2296	2301	2307	2312	2317	2323	2328	2333	2339	0	0	1	1	1	1	1	1	1	
.37	2344	2349	2354	2359	2365	2370	2375	2380	2386	2391	0	0	1	1	1	1	1	1	1	
.38	2399	2404	2410	2415	2421	2427	2432	2438	2443	2449	0	0	1	1	1	1	1	1	1	
.39	2455	2460	2466	2472	2477	2483	2489	2495	2500	2506	0	0	1	1	1	1	1	1	1	
.40	2512	2518	2523	2529	2535	2541	2547	2553	2559	2564	0	0	1	1	1	1	1	1	1	
.41	2570	2576	2582	2588	2594	2600	2606	2612	2618	2624	0	0	1	1	1	1	1	1	1	
.42	2629	2635	2641	2647	2653	2659	2665	2671	2677	2683	0	0	1	1	1	1	1	1	1	
.43	2689	2695	2701	2707	2713	2719	2725	2731	2737	2743	0	0	1	1	1	1	1	1	1	
.44	2754	2761	2767	2773	2779	2786	2792	2798	2804	2811	0	0	1	1	1	1	1	1	1	
.45	2818	2825	2831	2838	2844	2851	2858	2864	2871	2877	0	0	1	1	1	1	1	1	1	
.46	2884	2891	2897	2904	2911	2917	2924	2931	2938	2944	0	0	1	1	1	1	1	1	1	
.47	2951	2958	2965	2972	2979	2986	2992	2999	3006	3013	0	0	1	1	1	1	1	1	1	
.48	3020	3027	3034	3041	3048	3055	3062	3069	3076	3083	0	0	1	1	1	1	1	1	1	
.49	3090	3097	3105	3112	3119	3126	3133	3141	3148	3155	0	0	1	1	1	1	1	1	1	
.50	3162	3170	3177	3184	3192	3199	3206	3214	3221	3228	0	0	1	1	1	1	1	1	1	
.51	3236	3243	3251	3258	3265	3273	3280	3287	3295	3302	0	0	1	1	1	1	1	1	1	
.52	3311	3319	3327	3334	3342	3350	3357	3365	3373	3381	0	0	1	1	1	1	1	1	1	
.53	3388	3396	3404	3412	3420	3428	3436	3443	3451	3459	0	0	1	1	1	1	1	1	1	
.54	3467	3475	3483	3491	3499	3508	3516	3524	3532	3540	0	0	1	1	1	1	1	1	1	
.55	3548	3556	3565	3573	3581	3589	3597	3606	3614	3622	0	0	1	1	1	1	1	1	1	
.56	3631	3639	3648	3656	3664	3673	3681	3690	3698	3707	0	0	1	1	1	1	1	1	1	
.57	3715	3724	3733	3741	3750	3758	3767	3776	3784	3793	0	0	1	1	1	1	1	1	1	
.58	3803	3811	3819	3828	3837	3846	3855	3864	3873	3882	0	0	1	1	1	1	1	1	1	
.59	3890	3899	3908	3917	3926	3936	3945	3954	3963	3972	0	0	1	1	1	1	1	1	1	
.60	3981	3990	3999	4009	4018	4027	4036	4046	4055	4064	0	0	1	1	1	1	1	1	1	
.61	4074	4083	4093	4102	4111	4121	4130	4140	4149	4159	0	0	1	1	1	1	1	1	1	
.62	4169	4178	4188	4198	4207	4217	4226	4236	4246	4256	0	0	1	1	1	1	1	1	1	
.63	4266	4276	4285	4295	4305	4315	4325	4335	4345	4355	0	0	1	1	1	1	1	1	1	
.64	4365	4375	4385	4395	4406	4416	4426	4436	4446	4457	0	0	1	1	1	1	1	1	1	
.65	4467	4477	4487	4498	4508	4519	4529	4539	4550	4560	0	0	1	1	1	1	1	1	1	
.66	4571	4581	4592	4603	4613	4624	4635	4646	4657	4668	0	0	1	1	1	1	1	1	1	
.67	4677	4688	4699	4710	4721	4732	4743	4754	4766	4777	0	0	1	1	1	1	1	1	1	
.68	4788	4797	4808	4819	4831	4842	4853	4864	4875	4887	0	0	1	1	1	1	1	1	1	
.69	4898	4909	4920	4932	4943	4955	4966	4977	4989	5000	0	0	1	1	1	1	1	1	1	
.70	5012	5023	5035	5047	5058	5070	5082	5093	5105	5117	0	0	1	1	1	1	1	1	1	
.71	5129	5140	5152	5164	5176	5188	5200	5212	5224	5236	0	0	1	1	1	1	1	1	1	
.72	5248	5260	5272	5284	5297	5309	5321	5333	5346	5358	0	0	1	1	1	1	1	1	1	
.73	5370	5383	5395	5408	5420	5433	5445	5458	5470	5483	0	0	1	1	1	1	1	1	1	
.74	5495	5508	5521	5534	5546	5559	5572	5585	5598	5610	0	0	1	1	1	1	1	1	1	
.75	5623	5636	5649	5662	5675	5688	5702	5715	5728	5741	0	0	1	1	1	1	1	1	1	
.76	5754	5768	5781	5794	5808	5821	5834	5848	5861	5875										

x	0.000	0.001	0.002	0.003	0.004	0.005	0.006	0.007	0.008	0.009
0.000	—	—	—	—	—	—	—	—	—	—
010	—4.60517	—4.50986	—4.42285	—4.34281	—4.26870	—4.19971	—4.13517	—4.07454	—4.01738	—3.96332
020	—3.91202	—3.86323	—3.81671	—3.77226	—3.72970	—3.68888	—3.64966	—3.61192	—3.57555	—3.54046
030	50656	47377	44202	41125	38139	35241	32424	29684	27017	24419
040	21888	19418	17009	14656	12357	10109	7911	5761	3655	1593
0.050	—2.99573	—2.97593	—2.95651	—2.93746	—2.91877	—2.90042	—2.88240	—2.86470	—2.84731	—2.83022
060	81341	79688	78062	76462	74887	73337	71810	70306	68825	67365
070	65926	64508	63109	61730	60369	59027	57702	56395	55105	53831
080	52573	51331	50104	48891	47694	46510	45341	44185	43042	41912
090	40795	39690	38597	37516	36446	35388	34341	33304	32279	31264
0.100	—2.30259	—2.29263	—2.28278	—2.27303	—2.26336	—2.25379	—2.24432	—2.23493	—2.22562	—2.21641
110	20727	19823	18926	18037	17156	16282	15417	14558	13707	12863
120	12026	11196	10373	9557	8747	7944	7147	6357	5573	4794
130	04022	03256	02495	01741	00992	00248	—1.99510	—1.98777	—1.98050	—1.97328
140	—1.96611	—1.95900	—1.95193	—1.94491	—1.93794	—1.93102	—1.92415	—1.91732	—1.91054	—1.90381
150	—1.89712	—1.89048	—1.88387	—1.87732	—1.87080	—1.86433	—1.85790	—1.85151	—1.84516	—1.83885
160	83258	82635	82016	81401	80789	80181	79577	78976	78379	77786
170	71196	70609	70026	75446	74870	74297	73727	73161	72597	72037
180	71480	70926	70375	69827	69282	68740	68201	67665	67131	66601
190	66073	65548	65026	64507	63990	63476	62964	62455	61949	61445
0.200	—1.60944	—1.60445	—1.59949	—1.59455	—1.58964	—1.58475	—1.57988	—1.57504	—1.57022	—1.56542
210	56065	55590	55117	54646	54178	53712	53248	52786	52326	51868
220	51413	50939	50468	50000	49535	49072	48611	48151	47691	47233
230	46968	46534	46102	45672	45244	44817	44392	43967	43543	43120
240	42712	42296	41882	41469	41059	40650	40242	39837	39433	39030
0.250	—1.38629	—1.38230	—1.37833	—1.37437	—1.37042	—1.36649	—1.36258	—1.35868	—1.35480	—1.35093
260	34707	34323	33941	33560	33181	32803	32426	32051	31677	31304
270	30933	30564	30195	29828	29463	29098	28735	28374	28013	27654
280	27297	26940	26585	26231	25878	25527	25176	24827	24479	24133
290	23787	23443	23100	22758	22418	22078	21740	21402	21066	20731
0.300	—1.20397	—1.20065	—1.19733	—1.19402	—1.19073	—1.18744	—1.18417	—1.18091	—1.17766	—1.17441
310	17118	16796	16475	16155	15836	15518	15201	14885	14570	14256
320	13943	13631	13320	13010	12701	12393	12086	11780	11474	11170
330	10866	10564	10262	9961	9661	9362	9064	8767	8471	8176
340	07881	07587	07294	07002	06711	06421	06132	05843	05555	05268
0.350	—1.04982	—1.04697	—1.04412	—1.04129	—1.03846	—1.03564	—1.03282	—1.03002	—1.02722	—1.02443
360	02165	01888	01611	01335	01060	00786	00512	00239	—0.09967	—0.99696
370	—0.99425	—0.99155	—0.98886	—0.98618	—0.98350	—0.98083	—0.97817	—0.97551	—0.97286	—0.97022
380	96758	96496	96233	95972	95711	95451	95191	94933	94675	94418
390	94161	93905	93649	93395	93140	92887	92634	92382	92130	91879
0.400	—0.91629	—0.91379	—0.91130	—0.90882	—0.90634	—0.90387	—0.90140	—0.89894	—0.89649	—0.89404
410	89160	88916	88673	88431	88189	87948	87707	87467	87227	86988
420	86750	86512	86275	86038	85802	85567	85332	85097	84863	84630
430	84397	84165	83933	83702	83471	83241	83011	82782	82554	82326
440	82098	81871	81645	81419	81193	80968	80744	80520	80296	80073
0.450	—0.79851	—0.79629	—0.79407	—0.79186	—0.78966	—0.78746	—0.78526	—0.78307	—0.78089	—0.77871
460	77653	77436	77219	77003	76787	76572	76357	76143	75929	75715
470	75502	75290	75078	74866	74655	74444	74234	74024	73814	73605
480	73397	73189	72981	72774	72567	72361	72155	71949	71744	71539
490	71335	71131	70928	70725	70522	70320	70118	69917	69716	69515
0.500	—0.69315	—0.69115	—0.68918	—0.68717	—0.68518	—0.68320	—0.68122	—0.67924	—0.67727	—0.67531
510	67334	67139	66943	66748	66553	66359	66165	65971	65778	65585
520	65393	65201	65009	64817	64626	64436	64245	64055	63866	63677
530	63488	63299	63111	62923	62736	62549	62362	62176	61990	61804
540	61619	61434	61249	61065	60881	60697	60514	60331	60148	59966
0.550	—0.59784	—0.59602	—0.59421	—0.59240	—0.59059	—0.58879	—0.58699	—0.58519	—0.58340	—0.58161
560	57982	57803	57625	57448	57270	57093	56916	56740	56563	56387
570	56212	56037	55862	55687	55513	55339	55165	54991	54818	54645
580	54473	54300	54128	53957	53785	53614	53442	53270	53103	52933
590	52763	52594	52425	52256	52088	51919	51751	51584	51416	51249
0.600	—0.51083	—0.50916	—0.50750	—0.50584	—0.50418	—0.50253	—0.50088	—0.49923	—0.49758	—0.49594
610	49430	49266	49102	48939	48776	48613	48451	48289	48127	47965
620	47804	47642	47482	47321	47160	47000	46840	46681	46522	46362
630	46204	46045	45887	45728	45571	45413	45256	45099	44942	44785
640	44629	44473	44317	44161	44006	43850	43695	43541	43386	43232
0.650	—0.43078	—0.42925	—0.42771	—0.42618	—0.42465	—0.42312	—0.42159	—0.42007	—0.41855	—0.41703
660	41552	41400	41249	41098	40947	40797	40647	40497	40347	40197
670	40048	39899	39750	39601	39453	39304	39156	39008	38860	38713
680	38566	38419	38273	38126	37980	37834	37688	37542	37397	37251
690	37106	36962	36817	36673	36528	36384	36241	36097	35954	35810
0.700	—0.35667	—0.35525	—0.35382	—0.35240	—0.35098	—0.34956	—0.34814	—0.34672	—0.34531	—0.34390
710	34249	34108	33968	33827	33687	33547	33408	33268	33129	32989
720	32850	32712	32573	32435	32296	32158	32021	31883	31745	31608
730	31471	31334	31197	31061	30925	30788	30653	30517	30381	30246
740	30111	29975	29841	29706	29571	29437	29303	29169	29035	28902
0.750	—0.28768	—0.28635	—0.28502	—0.28369	—0.28236	—0.28104	—0.27971	—0.27839	—0.27707	—0.27575
760	27444	27312	27181	27050	26919	26788	26657	26527	26397	26266
770	26136	26007	25877	25748	25618	25489	25360	25231	25103	24974
780	24846	24718	24590	24462	24335	24207	24080	23953	23826	23699
790	23572	23446	23319	23193	23067	22941	22816	22690	22565	22439
0.800	—0.22314	—0.22189	—0.22065	—0.21940	—0.21816	—0.21691	—0.21567	—0.21443	—0.21319	—0.21196
810	21072	20949	20825	20702	20579	20457	20334	20212	20089	19967
820	19845	19723	19601	19480	19358	19237	19116	18995	18874	18754
830	18633	18513	18392	18272	18152	18032	17913	17793	17674	17554
840	17435	17316	17198	17079	16960	16842	16724	16605	16487	16369
0.850	—0.16252	—0.16134	—0.16017	—0.15900	—0.15782	—0.15665	—0.15548	—0.15432	—0.15315	—0.15199
860	15032	14966	14850	14734	14618	14503	14387	14272	14156	14041
870	13926	13811	13697	13582	13467	13353	13239	13125	13011	12897
880	12783	12670	12556	12443	12330	12217	12104	11991	11878	11766
890	11653	11541	11429	11317	11205	11093	10981	10870	10759	10647
0.900	—0.10536	—0.10425	—0.10314	—0.10203	—0.10092	—0.09982	—0.09871	—0.09761	—0.09651	—0.09541
910	09431	09321	09212	09102	08992	08883	08774	08665	08556	08447
920	08338	08230	08121	08013	07904	07796	07688	07580	07472	07365
930	07257	07150	07042	06935	06828	06721	06614	06507	06401	06294
940	06188	06081	05975	05869	05763	05657	05551	05446	05340	05235
0.950	—0.05129	—0.05024	—0.04919	—0.04814	—0.04709	—0.04604	—0.04500	—0.04395	—0.04291	—0.04186
960	04082	03978	03874	03770	03666	03563	03459	03356	03252	03149
970	03046	02943	02840	02737	02634	02532	02429	02327	02225	02122
980	02020	01918	01816	01714	01612	01510	01408	01306	01204	01102
990	01000	00900	00800	00700	00600	00500	00400	00300	00200	00100

x	0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09
1.00	0.00000	0.00095	0.00190	0.00285	0.00379	0.00473	0.00567	0.00661	0.00756	0.00851
10	0.9531	1.0333	1.1133	1.1933	1.2733	1.3533	1.4333	1.5133	1.5933	1.6733
20	18.232	19.623	21.013	22.403	23.793	25.183	26.573	27.963	29.353	30.743
30	26.236	27.703	29.170	30.637	32.104	33.571	35.038	36.505	37.972	39.439
40	336.47	34359	35066	35767	36464	37156	37844	38526	39204	39878
1.50	0.40547	0.41211	0.41871	0.42527	0.43178	0.43825	0.44468	0.45108	0.45745	0.46373
60	47000	47623	48243	48858	49470	50078	50682	51282	51879	52473
70	53063	53649	54232	54812	55389	55962	56531	57098	57661	58222
80	58778	59333	59884	60432	60977	61519	62058	62594	63127	63658
90	64183	64710	65233	65752	66269	66783	67294	67803	68310	68813
2.00	0.69315	0.69813	0.70310	0.70804	0.71295	0.71784	0.72271	0.72755	0.73237	0.73716
10	74194	74690	75182	75671	76158	76643	77125	77604	78081	78556
20	78846	79299	79751	80200	80648	81093	81536	81978	82418	82855
30	83291	83725	84157	84587	85015	85442	85866	86289	86710	87129
40	87547	87963	88377	88789	89199	89606	90011	90414	90816	91217
2.50	0.91629	0.92028	0.92426	0.92822	0.93216	0.93609	0.94000	0.94391	0.94779	0.95166
60	95551	95935	96317	96698	97078	97456	97832	98208	98582	98954
70	99325	99695	1.00063	1.00430	1.00795	1.01158	1.01519	1.01878	1.02235	1.02590
80	1.02945	1.03318	1.03687	1.04054	1.04419	1.04782	1.05143	1.05502	1.05859	1.06214
90	0.6471	0.6515	0.6558	0.6601	0.6643	0.6685	0.6727	0.6768	0.6809	0.6850
3.00	1.09861	1.10194	1.10525	1.10855	1.11186	1.11514	1.11841	1.12168	1.12493	1.12817
10	13140	13462	13783	14103	14422	14740	15057	15373	15688	16002
20	16315	16627	16938	17248	17557	17865	18173	18479	18784	19089
30	19392	19695	19996	20297	20597	20896	21194	21491	21788	22083
40	22378	22671	22964	23256	23547	23837	24127	24415	24703	24990
3.50	1.25276	1.25562	1.25846	1.26130	1.26413	1.26695	1.26976	1.27255	1.27533	1.27811
60	28093	28371	28647	28923	29199	29473	29746	30019	30291	30563
70	30833	31103	31372	31641	31909	32176	32442	32708	32973	33237
80	33500	33763	34025	34286	34547	34807	35067	35325	35584	35841
90	36098	36354	36609	36864	37118	37372	37624	37877	38128	38379
4.00	1.38629	1.38879	1.39128	1.39377	1.39624	1.39872	1.40118	1.40367	1.40614	1.40854
10	41829	41829	41829	41829	41829	41829	41829	41829	41829	41829
20	43508	43746	43984	44222	44456	44692	44927	45161	45395	45629
30	45862	46094	46326	46557	46787	47018	47247	47476	47705	47933
40	48160	48387	48614	48840	49065	49290	49515	49739	49962	50185
4.50	1.50408	1.50630	1.50851	1.51072	1.51293	1.51513	1.51732	1.51951	1.52170	1.52388
60	52606	52823	53039	53256	53471	53687	53902	54116	54330	54543
70	54756	54969	55181	55393	55604	55814	56024	56233	56442	56650
80	56852	57070	57287	57503	57718	57933	58147	58360	58573	58785
90	58994	59217	59431	59644	59857	60069	60281	60492	60703	60914
5.00	1.60944	1.61144	1.61343	1.61542	1.61741	1.61939	1.62137	1.62334	1.62531	1.62728
10	62924	63120	63315	63511	63706	63900	64094	64287	64481	64673
20	64866	65058	65250	65441	65632	65823	66013	66203	66393	66582
30	66771	66959	67147	67335	67522	67709	67896	68083	68269	68455
40	68640	68825	69010	69194	69378	69562	69745	69928	70111	70293
5.50	1.70475	1.70656	1.70838	1.71019	1.71199	1.71380	1.71560	1.71740	1.71919	1.72098
10	72277	72455	72633	72811	72989	73166	73342	73519	73695	73871
20	74047	74222	74397	74572	74746	74920	75094	75267	75440	75613
30	75788	75958	76128	76297	76464	76631	76798	76964	77130	77296
40	77455	77625	77794	77962	78130	78297	78464	78631	78798	78964
6.00	1.74176	1.74342	1.74508	1.74674	1.74839	1.75004	1.75169	1.75334	1.75499	1.75664
10	80829	80993	81157	81321	81484	81648	81811	81974	82137	82299
20	82455	82618	82781	82944	83107	83269	83432	83594	83757	83919
30	84085	84241	84397	84553	84708	84863	85018	85173	85327	85482
40	85630	85786	85941	86096	86251	86406	86561	86716	86871	87026
6.50	1.87180	1.87334	1.87487	1.87641	1.87794	1.87947	1.88099	1.88251	1.88403	1.88555
60	88707	88860	89013	89166	89318	89471	89623	89775	89927	90079
70	90231	90383	90535	90687	90839	90991	91142	91294	91446	91598
80	91699	91851	91999	92147	92295	92443	92591	92738	92886	93033
90	93182	93329	93476	93623	93769	93916	94062	94209	94355	94502
7.00	1.94591	1.94734	1.94876	1.95019	1.95161	1.95303	1.95445	1.95586	1.95727	1.95869
10	96009	96150	96291	96431	96571	96711	96851	96991	97130	97269
20	97408	97547	97685	97824	97962	98100	98238	98376	98513	98651
30	98787	98924	99061	99198	99334	99471	99607	99743	99879	1.00013
40	2.00148	2.00283	2.00418	2.00553	2.00687	2.00821	2.00955	2.01089	2.01223	2.01357
7.50	2.01430	2.01624	2.01817	2.02010	2.02202	2.02395	2.02587	2.02779	2.02971	2.03163
60	0.2815	0.2946	0.3076	0.3206	0.3336	0.3466	0.3596	0.3726	0.3856	0.3986
70	0.4122	0.4252	0.4381	0.4511	0.4640	0.4769	0.4898	0.5027	0.5156	0.5285
80	0.5413	0.5540	0.5668	0.5796	0.5924	0.6051	0.6179	0.6306	0.6433	0.6560
90	0.6686	0.6813	0.6939	0.7065	0.7191	0.7317	0.7443	0.7568	0.7694	0.7819
8.00	2.07944	2.08069	2.08194	2.08318	2.08443	2.08567	2.08691	2.08815	2.08939	2.09063
10	0.9186	0.9191	0.9196	0.9201	0.9206	0.9211	0.9216	0.9221	0.9226	0.9231
20	10.343	10.535	10.727	10.919	11.111	11.303	11.495	11.687	11.879	12.071
30	11626	11745	11864	11983	12102	12221	12340	12459	12578	12697
40	12813	12942	13071	13200	13329	13458	13587	13716	13845	13974
8.50	2.14007	2.14124	2.14242	2.14359	2.14476	2.14593	2.14710	2.14827	2.14943	2.15060
60	15176	15292	15409	15525	15641	15757	15873	15989	16105	16221
70	16332	16447	16562	16677	16792	16907	17022	17137	17252	17367
80	17475	17589	17702	17816	17929	18043	18157	18270	18384	18497
90	18605	18717	18830	18942	19054	19166	19277	19389	19500	19611
9.00	2.19722	2.19834	2.19944	2.20055	2.20166	2.20276	2.20387	2.20497	2.20607	2.20717
10	20827	20937	21047	21157	21266	21375	21484	21593	21702	21811
20	21920	22029	22138	22246	22355	22463	22571	22679	22787	22895
30	23001	23109	23216	23324	23431	23538	23645	23752	23859	23966
40	24071	24177	24284	24390	24496	24601	24707	24813	24918	25024
9.50	2.25129	2.25234	2.25339	2.25444	2.25548	2.25652	2.25756	2.25860	2.25964	2.26067
60	26176	26280	26384	26488	26592	26696	26799	26903	27007	27110
70	27213	27316	27419	27522	27625	27728	27831	27934	28037	28140
80	28243	28346	28448	28551	28653	28756	28858	28961	29063	29165
90	29267	29369	29471	29573	29675	29777	29879	29981	30083	30185

* To find the natural logarithm (\log_e) of a number which is a power of ten less or greater than a number given in the table, at the number concerned is less, e.g., $\log_e (10^{-1}) = \log_e (10) - 1$, $\log_e (10^{-2}) = \log_e (10) - 2$, etc., subtract from the given logarithm $\log_e 10$, 2 $\log_e 10$, 3 $\log_e 10$, etc., if the number concerned is greater, e.g., $\log_e 10$

times (10^1), 10 times (10^2), 100 times (10^3), etc. Examples: $\log_e 0.02 = \log_e 2 - 2 \log_e 10$, $\log_e 2000 = \log_e 200 + 3 \log_e 10$

N	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
10.0	2.30259	2.31254	2.32239	2.33214	2.34181	2.35138	2.36085	2.37024	2.37955	2.38876
11.0	39790	40695	41591	42480	43361	44235	45101	45959	46810	47654
12.0	48491	49321	50144	50960	51770	52573	53370	54160	54945	55723
13.0	56495	57261	58022	58776	59525	60269	61007	61740	62467	63189
14.0	63906	64617	65324	66026	66723	67415	68102	68785	69463	70136
15.0	2.70805	2.71469	2.72130	2.72785	2.73437	2.74084	2.74727	2.75366	2.76001	2.76632
16.0	77259	77882	78501	79117	79728	80336	80940	81541	82138	82731
17.0	83321	83908	84491	85071	85647	86220	86790	87356	87920	88480
18.0	89037	89591	90142	90690	91235	91777	92316	92852	93386	93916
19.0	94444	94969	95491	96011	96527	97041	97553	98062	98568	99072
20.0	2.99573	3.00072	3.00568	3.01062	3.01553	3.02042	3.02529	3.03013	3.03495	3.03975
21.0	3.04452	04927	05400	05871	06339	06805	07269	07731	08191	08649
22.0	09104	09558	10009	10459	10906	11352	11795	12236	12676	13114
23.0	13549	13983	14415	14845	15274	15700	16125	16548	16969	17388
24.0	17805	18221	18635	19048	19458	19867	20275	20680	21084	21487
25.0	3.21888	3.22287	3.22684	3.23080	3.23475	3.23868	3.24259	3.24649	3.25037	3.25424
26.0	25810	26194	26576	26957	27336	27714	28091	28466	28840	29213
27.0	29584	29953	30322	30689	31054	31419	31782	32143	32504	32863
28.0	33220	33577	33932	34286	34639	34990	35341	35690	36038	36384
29.0	36730	37074	37417	37759	38099	38439	38777	39115	39451	39786
30.0	3.40120	3.40453	3.40784	3.41115	3.41444	3.41773	3.42100	3.42426	3.42751	3.43076
31.0	43399	43721	44042	44362	44681	44999	45316	45632	45947	46261
32.0	46574	46886	47197	47507	47816	48124	48431	48738	49043	49347
33.0	49651	49953	50255	50556	50856	51155	51453	51750	52046	52342
34.0	52636	52930	53223	53515	53806	54096	54385	54674	54962	55249
35.0	3.55535	3.55820	3.56105	3.56388	3.56671	3.56953	3.57235	3.57515	3.57795	3.58074
36.0	58352	58629	58906	59182	59457	59731	60005	60278	60550	60821
37.0	61092	61362	61631	61899	62167	62434	62700	62966	63231	63495
38.0	63759	64021	64284	64546	64806	65066	65325	65584	65842	66099
39.0	66356	66612	66868	67122	67377	67630	67883	68135	68387	68638
40.0	3.68888	3.69138	3.69387	3.69635	3.69883	3.70130	3.70377	3.70623	3.70868	3.71113
41.0	71357	71601	71844	72086	72328	72569	72810	73050	73290	73529
42.0	73767	74005	74242	74479	74715	74950	75185	75420	75654	75887
43.0	76120	76352	76584	76815	77046	77276	77506	77735	77963	78191
44.0	78419	78646	78872	79098	79324	79549	79773	79997	80221	80444
45.0	3.80666	3.80888	3.81110	3.81331	3.81551	3.81771	3.81991	3.82210	3.82428	3.82647
46.0	82864	83081	83298	83514	83730	83945	84160	84374	84588	84802
47.0	85015	85227	85439	85651	85862	86073	86283	86493	86703	86912
48.0	87120	87328	87536	87743	87950	88156	88362	88568	88773	88978
49.0	89182	89386	89589	89792	89995	90197	90399	90600	90801	91002
50.0	3.91202	3.91402	3.91602	3.91801	3.91999	3.92197	3.92395	3.92593	3.92790	3.92986
51.0	93183	93378	93574	93769	93964	94158	94352	94546	94739	94932
52.0	95124	95316	95508	95700	95891	96081	96272	96462	96651	96840
53.0	97029	97218	97406	97594	97781	97968	98155	98341	98527	98713
54.0	98898	99083	99268	99452	99636	99820	4.00003	4.00186	4.00369	4.00551
55.0	4.00733	4.00915	4.01096	4.01277	4.01458	4.01638	4.01818	4.01998	4.02177	4.02356
56.0	02535	02714	02892	03069	03247	03424	03601	03777	03954	04130
57.0	04305	04480	04655	04830	05004	05178	05352	05526	05699	05872
58.0	06044	06217	06389	06560	06732	06903	07073	07244	07414	07584
59.0	07754	07923	08092	08261	08429	08598	08766	08933	09101	09268
60.0	4.09434	4.09601	4.09767	4.09933	4.10099	4.10264	4.10429	4.10594	4.10759	4.10923
61.0	11087	11251	11415	11578	11741	11904	12066	12228	12390	12552
62.0	12713	12875	13036	13196	13357	13517	13677	13836	13996	14155
63.0	14313	14472	14630	14789	14946	15104	15261	15418	15575	15732
64.0	15888	16044	16200	16356	16511	16667	16821	16976	17131	17285
65.0	4.17439	4.17592	4.17746	4.17899	4.18052	4.18205	4.18358	4.18510	4.18662	4.18814
66.0	18965	19117	19268	19419	19570	19720	19870	20020	20170	20320
67.0	20469	20618	20767	20916	21065	21213	21361	21509	21656	21804
68.0	21951	22098	22244	22391	22537	22683	22829	22975	23120	23266
69.0	23411	23555	23700	23844	23989	24133	24276	24420	24563	24707
70.0	4.24850	4.24992	4.25135	4.25277	4.25419	4.25561	4.25703	4.25845	4.25986	4.26127
71.0	26268	26409	26549	26690	26830	26970	27110	27249	27388	27528
72.0	27667	27805	27944	28082	28221	28359	28496	28634	28772	28910
73.0	29046	29183	29320	29456	29592	29729	29865	30000	30136	30271
74.0	30407	30542	30676	30811	30946	31080	31214	31348	31482	31615
75.0	4.31749	4.31882	4.32015	4.32149	4.32281	4.32413	4.32546	4.32678	4.32810	4.32942
76.0	33073	33205	33336	33467	33598	33729	33860	33990	34120	34251
77.0	34381	34510	34640	34769	34899	35028	35157	35286	35414	35543
78.0	35671	35800	35927	36055	36182	36310	36437	36564	36691	36818
79.0	36945	37071	37198	37324	37450	37576	37701	37827	37952	38078
80.0	4.38203	4.38328	4.38452	4.38577	4.38701	4.38826	4.38950	4.39074	4.39198	4.39321
81.0	39445	39568	39692	39815	39938	40060	40183	40305	40428	40550
82.0	40672	40794	40916	41037	41159	41280	41401	41522	41643	41764
83.0	41884	42004	42125	42245	42365	42485	42604	42724	42843	42963
84.0	43082	43201	43319	43438	43557	43675	43793	43912	44030	44147
85.0	4.44265	4.44383	4.44500	4.44617	4.44735	4.44852	4.44969	4.45085	4.45202	4.45318
86.0	45435	45551	45667	45783	45899	46014	46130	46245	46361	46476
87.0	46591	46706	46820	46935	47050	47164	47278	47392	47506	47620
88.0	47734	47847	47961	48074	48187	48300	48413	48526	48639	48751
89.0	48864	48976	49088	49200	49312	49424	49536	49647	49758	49870
90.0	4.49981	4.50092	4.50203	4.50314	4.50424	4.50535	4.50645	4.50756	4.50866	4.50976
91.0	51086	51196	51305	51415	51525	51634	51743	51852	51961	52070
92.0	52179	52287	52396	52504	52613	52721	52829	52937	53045	53152
93.0	53260	53367	53475	53582	53689	53796	53903	54010	54116	54223
94.0	54329	54436	54542	54648	54754	54860	54966	55071	55177	55282
95.0	4.55388	4.55493	4.55598	4.55703	4.55808	4.55913	4.56017	4.56122	4.56226	4.56331
96.0	56435	56539	56643	56747	56851	56954	57058	57161	57265	57368
97.0	57471	57574	57677	57780	57883	57985	58088	58190	58292	58395
98.0	58497	58599	58701	58802	58904	59006	59107	59208	59310	59411
99.0	59512	59613	59714	59815	59915	60016	60116	60217	60317	60417

* To find the natural logarithm (\log_e) of a number which is a power of ten less or greater than a number given in the table: if the number concerned is *less*, e.g., $\frac{1}{10}$ (10^{-1}), $\frac{1}{100}$ (10^{-2}), $\frac{1}{1000}$ (10^{-3}), etc., *subtract* from the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc.; if the number concerned is *greater*, e.g., 10

times (10^1), 100 times (10^2), 1000 times (10^3), etc., *add* to the given logarithm $\log_e 10$, $2 \log_e 10$, $3 \log_e 10$, etc. Examples: $\log_e 0.02 = \log_e 0.2 - \log_e 10$; $\log_e 2000 = \log_e 200 + \log_e 10$.

x	0	1	2	3	4	5	6	7	8	9
00	∞	0.00000	0.69315	1.09861	1.38629	1.60946	1.79176	1.94591	2.07944	2.19722
10	2.30259	2.39790	2.48490	2.56315	2.63291	2.69525	2.75025	2.80799	2.86754	2.92889
20	2.99233	3.04522	3.09184	3.13249	3.16749	3.20705	3.25130	3.29944	3.35168	3.40822
30	3.45933	3.51488	3.56454	3.61851	3.66699	3.71918	3.77529	3.83562	3.89947	3.96714
40	4.01909	4.07247	4.12088	4.16451	4.20356	4.24823	4.28872	4.33532	4.37832	4.42792
50	4.47441	4.51811	4.55832	4.59523	4.62914	4.66035	4.68906	4.71547	4.74088	4.76549
60	4.78940	4.81181	4.83282	4.85253	4.87094	4.88815	4.90426	4.91937	4.93358	4.94689
70	4.95930	4.97181	4.98352	4.99443	5.00464	5.01425	5.02326	5.03167	5.03948	5.04669
80	5.05330	5.05981	5.06582	5.07143	5.07664	5.08145	5.08586	5.09007	5.09408	5.09789
90	5.10150	5.10501	5.10822	5.11113	5.11384	5.11635	5.11866	5.12077	5.12268	5.12439
100	5.12590	5.12721	5.12832	5.12923	5.12994	5.13055	5.13106	5.13147	5.13178	5.13209
110	5.13230	5.13251	5.13262	5.13273	5.13284	5.13295	5.13306	5.13317	5.13328	5.13339
120	5.13350	5.13361	5.13372	5.13383	5.13394	5.13405	5.13416	5.13427	5.13438	5.13449
130	5.13460	5.13471	5.13482	5.13493	5.13504	5.13515	5.13526	5.13537	5.13548	5.13559
140	5.13570	5.13581	5.13592	5.13603	5.13614	5.13625	5.13636	5.13647	5.13658	5.13669
150	5.13680	5.13691	5.13702	5.13713	5.13724	5.13735	5.13746	5.13757	5.13768	5.13779
160	5.13790	5.13801	5.13812	5.13823	5.13834	5.13845	5.13856	5.13867	5.13878	5.13889
170	5.13900	5.13911	5.13922	5.13933	5.13944	5.13955	5.13966	5.13977	5.13988	5.13999
180	5.14010	5.14021	5.14032	5.14043	5.14054	5.14065	5.14076	5.14087	5.14098	5.14109
190	5.14120	5.14131	5.14142	5.14153	5.14164	5.14175	5.14186	5.14197	5.14208	5.14219
200	5.14230	5.14241	5.14252	5.14263	5.14274	5.14285	5.14296	5.14307	5.14318	5.14329
210	5.14340	5.14351	5.14362	5.14373	5.14384	5.14395	5.14406	5.14417	5.14428	5.14439
220	5.14450	5.14461	5.14472	5.14483	5.14494	5.14505	5.14516	5.14527	5.14538	5.14549
230	5.14560	5.14571	5.14582	5.14593	5.14604	5.14615	5.14626	5.14637	5.14648	5.14659
240	5.14670	5.14681	5.14692	5.14703	5.14714	5.14725	5.14736	5.14747	5.14758	5.14769
250	5.14780	5.14791	5.14802	5.14813	5.14824	5.14835	5.14846	5.14857	5.14868	5.14879
260	5.14890	5.14901	5.14912	5.14923	5.14934	5.14945	5.14956	5.14967	5.14978	5.14989
270	5.15000	5.15011	5.15022	5.15033	5.15044	5.15055	5.15066	5.15077	5.15088	5.15099
280	5.15110	5.15121	5.15132	5.15143	5.15154	5.15165	5.15176	5.15187	5.15198	5.15209
290	5.15220	5.15231	5.15242	5.15253	5.15264	5.15275	5.15286	5.15297	5.15308	5.15319
300	5.15330	5.15341	5.15352	5.15363	5.15374	5.15385	5.15396	5.15407	5.15418	5.15429
310	5.15440	5.15451	5.15462	5.15473	5.15484	5.15495	5.15506	5.15517	5.15528	5.15539
320	5.15550	5.15561	5.15572	5.15583	5.15594	5.15605	5.15616	5.15627	5.15638	5.15649
330	5.15660	5.15671	5.15682	5.15693	5.15704	5.15715	5.15726	5.15737	5.15748	5.15759
340	5.15770	5.15781	5.15792	5.15803	5.15814	5.15825	5.15836	5.15847	5.15858	5.15869
350	5.15880	5.15891	5.15902	5.15913	5.15924	5.15935	5.15946	5.15957	5.15968	5.15979
360	5.15990	5.16001	5.16012	5.16023	5.16034	5.16045	5.16056	5.16067	5.16078	5.16089
370	5.16100	5.16111	5.16122	5.16133	5.16144	5.16155	5.16166	5.16177	5.16188	5.16199
380	5.16210	5.16221	5.16232	5.16243	5.16254	5.16265	5.16276	5.16287	5.16298	5.16309
390	5.16320	5.16331	5.16342	5.16353	5.16364	5.16375	5.16386	5.16397	5.16408	5.16419
400	5.16430	5.16441	5.16452	5.16463	5.16474	5.16485	5.16496	5.16507	5.16518	5.16529
410	5.16540	5.16551	5.16562	5.16573	5.16584	5.16595	5.16606	5.16617	5.16628	5.16639
420	5.16650	5.16661	5.16672	5.16683	5.16694	5.16705	5.16716	5.16727	5.16738	5.16749
430	5.16760	5.16771	5.16782	5.16793	5.16804	5.16815	5.16826	5.16837	5.16848	5.16859
440	5.16870	5.16881	5.16892	5.16903	5.16914	5.16925	5.16936	5.16947	5.16958	5.16969
450	5.16980	5.16991	5.17002	5.17013	5.17024	5.17035	5.17046	5.17057	5.17068	5.17079
460	5.17090	5.17101	5.17112	5.17123	5.17134	5.17145	5.17156	5.17167	5.17178	5.17189
470	5.17200	5.17211	5.17222	5.17233	5.17244	5.17255	5.17266	5.17277	5.17288	5.17299
480	5.17310	5.17321	5.17332	5.17343	5.17354	5.17365	5.17376	5.17387	5.17398	5.17409
490	5.17420	5.17431	5.17442	5.17453	5.17464	5.17475	5.17486	5.17497	5.17508	5.17519
500	5.17530	5.17541	5.17552	5.17563	5.17574	5.17585	5.17596	5.17607	5.17618	5.17629
510	5.17640	5.17651	5.17662	5.17673	5.17684	5.17695	5.17706	5.17717	5.17728	5.17739
520	5.17750	5.17761	5.17772	5.17783	5.17794	5.17805	5.17816	5.17827	5.17838	5.17849
530	5.17860	5.17871	5.17882	5.17893	5.17904	5.17915	5.17926	5.17937	5.17948	5.17959
540	5.17970	5.17981	5.17992	5.18003	5.18014	5.18025	5.18036	5.18047	5.18058	5.18069
550	5.18080	5.18091	5.18102	5.18113	5.18124	5.18135	5.18146	5.18157	5.18168	5.18179
560	5.18190	5.18201	5.18212	5.18223	5.18234	5.18245	5.18256	5.18267	5.18278	5.18289
570	5.18300	5.18311	5.18322	5.18333	5.18344	5.18355	5.18366	5.18377	5.18388	5.18399
580	5.18410	5.18421	5.18432	5.18443	5.18454	5.18465	5.18476	5.18487	5.18498	5.18509
590	5.18520	5.18531	5.18542	5.18553	5.18564	5.18575	5.18586	5.18597	5.18608	5.18619
600	5.18630	5.18641	5.18652	5.18663	5.18674	5.18685	5.18696	5.18707	5.18718	5.18729
610	5.18740	5.18751	5.18762	5.18773	5.18784	5.18795	5.18806	5.18817	5.18828	5.18839
620	5.18850	5.18861	5.18872	5.18883	5.18894	5.18905	5.18916	5.18927	5.18938	5.18949
630	5.18960	5.18971	5.18982	5.18993	5.19004	5.19015	5.19026	5.19037	5.19048	5.19059
640	5.19070	5.19081	5.19092	5.19103	5.19114	5.19125	5.19136	5.19147	5.19158	5.19169
650	5.19180	5.19191	5.19202	5.19213	5.19224	5.19235	5.19246	5.19257	5.19268	5.19279
660	5.19290	5.19301	5.19312	5.19323	5.19334	5.19345	5.19356	5.19367	5.19378	5.19389
670	5.19400	5.19411	5.19422	5.19433	5.19444	5.19455	5.19466	5.19477	5.19488	5.19499
680	5.19510	5.19521	5.19532	5.19543	5.19554	5.19565	5.19576	5.19587	5.19598	5.19609
690	5.19620	5.19631	5.19642	5.19653	5.19664	5.19675	5.19686	5.19697	5.19708	5.19719
700	5.19730	5.19741	5.19752	5.19763	5.19774	5.19785	5.19796	5.19807	5.19818	5.19829
710	5.19840	5.19851	5.19862	5.19873	5.19884	5.19895	5.19906	5.19917	5.19928	5.19939
720	5.19950	5.19961	5.19972	5.19983	5.19994	5.20005	5.20016	5.20027	5.20038	5.20049
730	5.20060	5.20071	5.20082	5.20093	5.20104	5.20115	5.20126	5.20137	5.20148	5.20159
740	5.20170	5.20181	5.20192	5.20203	5.20214	5.20225	5.20236	5.20247	5.20258	5.20269
750	5.20280	5.20291	5.20302	5.20313	5.20324	5.20335	5.20346	5.20357	5.20368	5.20379
760	5.20390	5.20401	5.20412	5.20423	5.20434	5.20445	5.20456	5.20467	5.20478	5.20489
770	5.20500	5.20511	5.20522	5.20533	5.20544	5.20555	5.20566	5.20577	5.20588	5.20599
780	5.20610	5.20621	5.20632	5.20643	5.20654	5.20665	5.20676	5.20687	5.20698	5.20709
790	5.20720	5.20731	5.20742	5.20753	5.20764	5.20775	5.20786	5.20797	5.20808	5.20819
800	5.20830	5.20841	5.20852	5.20863	5.20874	5.20885	5.20896	5.20907	5.20918	5.20929
810	5.20940	5.20951	5.20962	5.20973	5.20984	5.20995	5.21006	5.21017	5.21028	5.21039
820	5.21050	5.21061	5.21072	5.21083	5.21094	5.21105	5.21116	5.21127	5.21138	5.21149
830	5.21160	5.21171	5.21182	5.21193	5.21204	5.21215	5.21226	5.21237	5.21248	5.21259
840	5.21270	5.21281	5.21292	5.21303	5.21314	5.21325	5.21336	5.21347	5.21358	5.21369
850	5.21380	5.21391	5.21402	5.21413	5.21424	5.21435	5.21446	5.21457	5.21468	5.21479
860	5.21490	5.21501	5.21512	5.21523	5.21534	5.21545	5.21556	5.21567	5.21578	5.21589
870	5.21600	5.21611	5.21622	5.21633	5.21644	5.21655	5.21666	5.21677	5.21688	5.21699
880	5.21710	5.21721	5.21732	5.21743	5.21754	5.21765	5.21776	5.21787	5.21798	5.21809
890	5.21820	5.21831	5.21842	5.21853	5.21864	5.21875	5.21886	5.21897	5.21908	5.21919
900	5.21930	5.21941	5.21952	5.21963	5.21974	5.21985	5.21996	5.22007	5.22018	5.22029
910	5.22040	5.22051	5.22062	5.22073	5.22084	5.22095	5.22106	5.22117	5.22128	5.22

x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}	x	e^x	$\log_{10}(e^x)$	e^{-x}
0.00	1.0000	0.00000	1.000000	1.00	2.7183	0.43429	0.367879	2.00	7.3891	0.86859	0.135335
0.01	1.0101	0.0434	0.990050	1.01	2.7456	43864	364219	2.01	7.4633	87293	133989
0.02	1.0202	0.0869	980199	1.02	2.7732	44298	360595	2.02	7.5383	87727	132655
0.03	1.0305	0.1303	970446	1.03	2.8011	44732	357007	2.03	7.6141	88162	131336
0.04	1.0408	0.1737	960789	1.04	2.8292	45167	353455	2.04	7.6906	88596	130029
0.05	1.0513	0.2171	0.951229	1.05	2.8577	0.45601	0.349938	2.05	7.7679	0.89030	0.128735
0.06	1.0618	0.2606	941765	1.06	2.8864	46035	346456	2.06	7.8460	89465	127454
0.07	1.0725	0.3040	932394	1.07	2.9154	46470	343009	2.07	7.9248	89899	126186
0.08	1.0833	0.3474	923116	1.08	2.9447	46904	339596	2.08	8.0045	90333	124930
0.09	1.0942	0.3909	913931	1.09	2.9743	47338	336216	2.09	8.0849	90768	123687
0.10	1.1052	0.4343	0.904837	1.10	3.0042	0.47772	0.332871	2.10	8.1662	0.91202	0.122456
0.11	1.1163	0.4777	895834	1.11	3.0344	48207	329599	2.11	8.2482	91636	121238
0.12	1.1275	0.5212	886920	1.12	3.0649	48641	326280	2.12	8.3311	92070	120032
0.13	1.1388	0.5646	878095	1.13	3.0957	49075	323033	2.13	8.4149	92505	118837
0.14	1.1503	0.6080	869358	1.14	3.1268	49510	319819	2.14	8.4994	92939	117655
0.15	1.1618	0.6514	0.860708	1.15	3.1582	0.49944	0.316637	2.15	8.5849	0.93373	0.116484
0.16	1.1735	0.6949	852144	1.16	3.1899	50378	313486	2.16	8.6711	93808	115325
0.17	1.1853	0.7383	843665	1.17	3.2220	50812	310367	2.17	8.7583	94242	114178
0.18	1.1972	0.7817	835270	1.18	3.2544	51247	307279	2.18	8.8463	94676	113042
0.19	1.2092	0.8252	826959	1.19	3.2871	51681	304221	2.19	8.9352	95110	111917
0.20	1.2214	0.8686	0.818731	1.20	3.3201	0.52115	0.301194	2.20	9.0250	0.95545	0.110803
0.21	1.2337	0.9120	810584	1.21	3.3535	52550	298197	2.21	9.1157	95979	109701
0.22	1.2461	0.9554	802519	1.22	3.3872	52984	295230	2.22	9.2073	96413	108609
0.23	1.2586	0.9989	794534	1.23	3.4212	53418	292293	2.23	9.2999	96848	107528
0.24	1.2712	1.0423	786628	1.24	3.4556	53853	289384	2.24	9.3933	97282	106459
0.25	1.2840	1.0857	0.778801	1.25	3.4903	0.54287	0.286505	2.25	9.4877	0.97716	0.105399
0.26	1.2969	1.1292	771052	1.26	3.5254	54721	283654	2.26	9.5831	98151	104350
0.27	1.3100	1.1726	763379	1.27	3.5609	55155	280832	2.27	9.6794	98585	103312
0.28	1.3231	1.2160	755784	1.28	3.5966	55590	278037	2.28	9.7767	99019	102284
0.29	1.3364	1.2595	748264	1.29	3.6328	56024	275271	2.29	9.8749	99453	101266
0.30	1.3499	0.13029	0.740818	1.30	3.6693	0.56458	0.272532	2.30	9.9742	0.99888	0.100259
0.31	1.3634	1.3463	733447	1.31	3.7062	56893	269820	2.31	10.074	1.00322	0.99261
0.32	1.3771	1.3771	726149	1.32	3.7434	57327	267135	2.32	10.176	0.0756	0.98274
0.33	1.3910	1.4332	718924	1.33	3.7810	57761	264477	2.33	10.278	0.1191	0.97296
0.34	1.4049	1.4766	711770	1.34	3.8190	58195	261846	2.34	10.381	0.1625	0.96328
0.35	1.4191	0.15200	0.704688	1.35	3.8574	0.58630	0.259240	2.35	10.486	1.02059	0.095369
0.36	1.4333	1.5635	697766	1.36	3.8962	59064	256661	2.36	10.591	0.2493	0.94420
0.37	1.4477	1.6069	690734	1.37	3.9354	59498	254107	2.37	10.697	0.2928	0.93481
0.38	1.4623	1.6503	683861	1.38	3.9749	59933	251579	2.38	10.805	0.3362	0.92551
0.39	1.4770	1.6937	677057	1.39	4.0149	60367	249075	2.39	10.913	0.3796	0.91630
0.40	1.4918	0.17372	0.670320	1.40	4.0552	0.60801	0.246597	2.40	11.023	1.04231	0.090718
0.41	1.5068	1.7806	663650	1.41	4.0960	61236	244143	2.41	11.134	0.4665	0.089815
0.42	1.5220	1.8240	657047	1.42	4.1371	61670	241714	2.42	11.246	0.5099	0.088922
0.43	1.5373	1.8675	650509	1.43	4.1787	62104	239309	2.43	11.359	0.5534	0.088037
0.44	1.5527	1.9109	644036	1.44	4.2207	62538	236928	2.44	11.473	0.5968	0.087161
0.45	1.5683	0.19543	0.637628	1.45	4.2631	0.62973	0.234570	2.45	11.588	1.06402	0.086294
0.46	1.5841	1.9978	631284	1.46	4.3060	63407	232236	2.46	11.705	0.6836	0.085435
0.47	1.6000	2.0412	625002	1.47	4.3492	63841	229925	2.47	11.822	0.7271	0.084585
0.48	1.6161	2.0846	618783	1.48	4.3929	64276	227638	2.48	11.941	0.7705	0.083743
0.49	1.6323	2.1280	612626	1.49	4.4371	64710	225373	2.49	12.061	0.8139	0.082910
0.50	1.6487	0.21715	0.606531	1.50	4.4817	0.65144	0.223130	2.50	12.182	1.08574	0.082085
0.51	1.6653	2.2149	600496	1.51	4.5267	65578	220910	2.51	12.305	0.9008	0.081268
0.52	1.6820	2.2583	594521	1.52	4.5722	66013	218712	2.52	12.429	0.9442	0.080460
0.53	1.6989	2.3018	588605	1.53	4.6182	66447	216536	2.53	12.554	0.9877	0.079659
0.54	1.7160	2.3452	582748	1.54	4.6646	66881	214381	2.54	12.680	1.0311	0.078866
0.55	1.7333	0.23886	0.576950	1.55	4.7115	0.67316	0.212248	2.55	12.807	1.10745	0.078082
0.56	1.7507	2.4320	571209	1.56	4.7588	67750	210136	2.56	12.936	1.1179	0.077305
0.57	1.7683	2.4755	565525	1.57	4.8066	68184	208045	2.57	13.066	1.1614	0.076536
0.58	1.7860	2.5189	559898	1.58	4.8550	68619	205975	2.58	13.197	1.2048	0.075774
0.59	1.8040	2.5623	554327	1.59	4.9037	69053	203926	2.59	13.330	1.2482	0.075020
0.60	1.8221	0.26058	0.548812	1.60	4.9530	0.69487	0.201897	2.60	13.464	1.12917	0.074274
0.61	1.8404	2.6492	543351	1.61	5.0028	69921	199888	2.61	13.599	1.17351	0.073535
0.62	1.8589	2.6926	537944	1.62	5.0531	70356	197899	2.62	13.736	1.21785	0.072803
0.63	1.8776	2.7361	532592	1.63	5.1039	70790	195930	2.63	13.874	1.26219	0.072078
0.64	1.8965	2.7795	527292	1.64	5.1552	71224	193980	2.64	14.013	1.30654	0.071361
0.65	1.9155	0.28229	0.522046	1.65	5.2070	0.71659	0.192050	2.65	14.154	1.15088	0.070651
0.66	1.9348	2.8663	516851	1.66	5.2593	72093	190139	2.66	14.296	1.19522	0.069948
0.67	1.9542	2.9098	511709	1.67	5.3122	72527	188247	2.67	14.440	1.23957	0.069252
0.68	1.9739	2.9532	506617	1.68	5.3656	72961	186374	2.68	14.585	1.28391	0.068563
0.69	1.9937	2.9966	501576	1.69	5.4195	73396	184520	2.69	14.732	1.32825	0.067881
0.70	2.0138	0.30401	0.496585	1.70	5.4739	0.73830	0.182684	2.70	14.880	1.17260	0.067206
0.71	2.0340	3.0835	491644	1.71	5.5290	74264	180866	2.71	15.029	1.21694	0.066537
0.72	2.0544	3.1269	486752	1.72	5.5845	74699	179066	2.72	15.180	1.26128	0.065875
0.73	2.0751	3.1703	481909	1.73	5.6407	75133	177284	2.73	15.333	1.30562	0.065219
0.74	2.0959	3.2138	477114	1.74	5.6973	75567	175520	2.74	15.487	1.35000	0.064570
0.75	2.1170	0.32572	0.472367	1.75	5.7546	0.76002	0.173774	2.75	15.643	1.19431	0.063928
0.76	2.1383	3.3006	467666	1.76	5.8124	76436	172045	2.76	15.800	1.23865	0.063292
0.77	2.1598	3.3441	463013	1.77	5.8709	76870	170333	2.77	15.959	1.28299	0.062662
0.78	2.1815	3.3875	458406	1.78	5.9299	77304	168638	2.78	16.119	1.32733	0.062039
0.79	2.2034	3.4309	453845	1.79	5.9895	77739	166960	2.79	16.281	1.37167	0.061421
0.80	2.2255	0.34744	0.449329	1.80	6.0496	0.78173	0.165299	2.80	16.445	1.21602	0.060810
0.81	2.2479	3.5174	444858	1.81	6.1104	78607	163654	2.81	16.610	1.26037	0.060205
0.82	2.2705	3.5612	440432	1.82	6.1719	79042	162026	2.82	16.777	1.30471	0.059606
0.83	2.2933	3.6046	436049	1.83	6.2339	79476	160414	2.83	16.945	1.34905	0.059013
0.84	2.3164	3.6481	431711	1.84	6.2965	79910	158817	2.84	17.116	1.39339	0.058426
0.85	2.3396	0.36915	0.427415	1.85	6.3598	0.80344	0.157237	2.85	17.287	1.23774	0.057844
0.86	2.3632	3.7349	423162	1.86	6.4237	80779	155673	2.86	17.462	1.28208	0.057269
0.87	2.3869	3.7784	418952	1.87	6.4883	81213	154124	2.87	17.637	1.32642	0.056699
0.88	2.4109	3.8218	414783	1.88	6.5535	81647	152590	2.88	17.814	1.37076	0.056135
0.89	2.4351	3.8652	410656	1.89	6.6194	82082	151072	2.89	17.993	1.41510	0.055576
0.90	2.4596	0.39087	0.406570	1.90	6.6859	0.82516	0.149569	2.90	18.174	1.25945	0.055023
0.91	2.4843	3.9521	40								

x	e^x	$\log_e(e^x)$	e^{-x}	x	e^x	$\log_e(e^x)$	e^{-x}	x	e^x	$\log_e(e^x)$	e^{-x}
1.00	20.086	1.30233	0.0473787	4.00	55.199	1.73178	0.018136	5.00	148.41	2.17147	0.006738
1.01	20.287	1.30273	0.046922	4.01	55.497	1.74152	0.018133	5.01	149.90	2.17542	0.006741
1.02	20.491	1.31157	0.046801	4.02	55.701	1.74586	0.017953	5.02	151.41	2.18014	0.006695
1.03	20.697	1.31591	0.046316	4.03	56.261	1.75021	0.017774	5.03	152.93	2.18430	0.006639
1.04	20.905	1.32026	0.046335	4.04	56.826	1.75454	0.017597	5.04	154.47	2.18894	0.006574
1.05	21.115	1.32460	0.047359	4.05	57.397	1.75889	0.017422	5.05	156.02	2.19391	0.006509
1.06	21.327	1.32894	0.046801	4.06	57.974	1.76324	0.017249	5.06	157.59	2.19924	0.006444
1.07	21.542	1.33328	0.046421	4.07	58.557	1.76758	0.017077	5.07	159.17	2.20487	0.006379
1.08	21.763	1.33763	0.045959	4.08	59.145	1.77192	0.016907	5.08	160.77	2.21062	0.006314
1.09	21.977	1.34197	0.045502	4.09	59.740	1.77626	0.016739	5.09	162.39	2.21656	0.006249
1.10	22.195	1.34631	0.045049	4.10	60.340	1.78061	0.016573	5.10	164.02	2.22240	0.006184
1.11	22.421	1.35066	0.044601	4.11	60.947	1.78495	0.016408	5.11	165.67	2.22824	0.006119
1.12	22.646	1.35500	0.044157	4.12	61.559	1.78929	0.016245	5.12	167.34	2.23419	0.006054
1.13	22.874	1.35934	0.043718	4.13	62.178	1.79364	0.016083	5.13	169.02	2.24027	0.005989
1.14	23.104	1.36368	0.043283	4.14	62.803	1.79798	0.015923	5.14	170.72	2.24627	0.005924
1.15	23.336	1.36803	0.042852	4.15	63.434	1.80232	0.015764	5.15	172.43	2.25226	0.005859
1.16	23.571	1.37237	0.042426	4.16	64.072	1.80667	0.015608	5.16	174.16	2.25826	0.005794
1.17	23.807	1.37671	0.042004	4.17	64.715	1.81101	0.015452	5.17	175.91	2.26426	0.005729
1.18	24.047	1.38106	0.041586	4.18	65.366	1.81535	0.015299	5.18	177.66	2.27026	0.005664
1.19	24.289	1.38540	0.041172	4.19	66.023	1.81969	0.015146	5.19	179.47	2.27626	0.005599
1.20	24.533	1.38974	0.040762	4.20	66.686	1.82404	0.014996	5.20	181.27	2.28226	0.005534
1.21	24.779	1.39409	0.040357	4.21	67.355	1.82838	0.014846	5.21	183.09	2.28826	0.005469
1.22	25.028	1.39843	0.039953	4.22	68.033	1.83272	0.014699	5.22	184.93	2.29426	0.005404
1.23	25.280	1.40277	0.039557	4.23	68.717	1.83707	0.014552	5.23	186.79	2.30026	0.005339
1.24	25.534	1.40711	0.039164	4.24	69.408	1.84141	0.014408	5.24	188.67	2.30626	0.005274
1.25	25.790	1.41146	0.038774	4.25	70.105	1.84575	0.014264	5.25	190.57	2.31226	0.005209
1.26	26.050	1.41581	0.038388	4.26	70.810	1.85009	0.014122	5.26	192.48	2.31826	0.005144
1.27	26.314	1.42014	0.038006	4.27	71.522	1.85444	0.013982	5.27	194.42	2.32426	0.005079
1.28	26.576	1.42449	0.037628	4.28	72.240	1.85878	0.013843	5.28	196.37	2.33026	0.005014
1.29	26.845	1.42883	0.037254	4.29	72.966	1.86312	0.013705	5.29	198.34	2.33626	0.004949
1.30	27.113	1.43317	0.036883	4.30	73.700	1.86747	0.013569	5.30	200.34	2.34226	0.004884
1.31	27.385	1.43751	0.036516	4.31	74.440	1.87181	0.013434	5.31	202.35	2.34826	0.004819
1.32	27.660	1.44185	0.036153	4.32	75.189	1.87615	0.013300	5.32	204.38	2.35426	0.004754
1.33	27.938	1.44620	0.035793	4.33	75.944	1.88050	0.013168	5.33	206.44	2.36026	0.004689
1.34	28.219	1.45054	0.035437	4.34	76.708	1.88484	0.013037	5.34	208.51	2.36626	0.004624
1.35	28.502	1.45489	0.035084	4.35	77.478	1.88918	0.012907	5.35	210.61	2.37226	0.004559
1.36	28.789	1.45923	0.034735	4.36	78.257	1.89352	0.012778	5.36	212.72	2.37826	0.004494
1.37	29.079	1.46357	0.034390	4.37	79.044	1.89787	0.012649	5.37	214.85	2.38426	0.004429
1.38	29.371	1.46792	0.034047	4.38	79.838	1.90221	0.012525	5.38	217.02	2.39026	0.004364
1.39	29.666	1.47226	0.033709	4.39	80.640	1.90655	0.012401	5.39	219.20	2.39626	0.004299
1.40	29.964	1.47660	0.033375	4.40	81.451	1.91090	0.012277	5.40	221.41	2.40226	0.004234
1.41	30.265	1.48094	0.033041	4.41	82.269	1.91524	0.012155	5.41	223.63	2.40826	0.004169
1.42	30.569	1.48529	0.032712	4.42	83.096	1.91958	0.012034	5.42	225.88	2.41426	0.004104
1.43	30.877	1.48963	0.032387	4.43	83.933	1.92392	0.011914	5.43	228.15	2.42026	0.004039
1.44	31.187	1.49397	0.032065	4.44	84.775	1.92827	0.011796	5.44	230.44	2.42626	0.003974
1.45	31.500	1.49832	0.031746	4.45	85.627	1.93261	0.011679	5.45	232.76	2.43226	0.003909
1.46	31.817	1.50266	0.031430	4.46	86.488	1.93695	0.011562	5.46	235.10	2.43826	0.003844
1.47	32.137	1.50700	0.031117	4.47	87.357	1.94130	0.011447	5.47	237.46	2.44426	0.003779
1.48	32.460	1.51134	0.030807	4.48	88.235	1.94564	0.011332	5.48	239.84	2.45026	0.003714
1.49	32.786	1.51568	0.030501	4.49	89.121	1.94998	0.011219	5.49	242.26	2.45626	0.003649
1.50	33.115	1.52003	0.030197	4.50	90.017	1.95433	0.011109				
1.51	33.448	1.52437	0.029897	4.51	90.922	1.95867	0.010998				
1.52	33.784	1.52872	0.029599	4.52	91.836	1.96301	0.010889				
1.53	34.124	1.53306	0.029303	4.53	92.759	1.96735	0.010781				
1.54	34.467	1.53740	0.029013	4.54	93.691	1.97170	0.010673	5.5	244.69	2.46226	0.003614
1.55	34.813	1.54175	0.028725	4.55	94.632	1.97604	0.010567	5.6	247.03	2.46826	0.003549
1.56	35.163	1.54609	0.028439	4.56	95.583	1.98038	0.010462	5.7	249.39	2.47426	0.003484
1.57	35.517	1.55043	0.028156	4.57	96.544	1.98473	0.010358	5.8	251.77	2.48026	0.003419
1.58	35.874	1.55478	0.027876	4.58	97.514	1.98907	0.010255	5.9	254.17	2.48626	0.003354
1.59	36.234	1.55912	0.027598	4.59	98.494	1.99341	0.010153	6.0	256.59	2.49226	0.003289
1.60	36.598	1.56346	0.027324	4.60	99.484	1.99775	0.010052	6.1	259.03	2.49826	0.003224
1.61	36.966	1.56780	0.027052	4.61	100.48	2.00209	0.009952	6.2	261.49	2.50426	0.003159
1.62	37.338	1.57213	0.026783	4.62	101.49	2.00643	0.009853	6.3	263.97	2.51026	0.003094
1.63	37.713	1.57647	0.026516	4.63	102.51	2.01078	0.009755	6.4	266.47	2.51626	0.003029
1.64	38.092	1.58081	0.026252	4.64	103.54	2.01513	0.009658	6.5	268.99	2.52226	0.002964
1.65	38.475	1.58515	0.025991	4.65	104.58	2.01947	0.009562	6.6	271.53	2.52826	0.002899
1.66	38.861	1.58952	0.025733	4.66	105.64	2.02381	0.009467	6.7	274.09	2.53426	0.002834
1.67	39.252	1.59386	0.025476	4.67	106.70	2.02816	0.009372	6.8	276.67	2.54026	0.002769
1.68	39.646	1.59820	0.025223	4.68	107.77	2.03250	0.009279	6.9	279.27	2.54626	0.002704
1.69	40.045	1.60254	0.024972	4.69	108.85	2.03684	0.009187	7.0	281.89	2.55226	0.002639
1.70	40.447	1.60689	0.024724	4.70	109.95	2.04118	0.009095	7.1	284.53	2.55826	0.002574
1.71	40.854	1.61123	0.024478	4.71	111.05	2.04553	0.009005	7.2	287.19	2.56426	0.002509
1.72	41.264	1.61558	0.024234	4.72	112.17	2.04987	0.008913	7.3	289.87	2.57026	0.002444
1.73	41.679	1.61992	0.023993	4.73	113.30	2.05421	0.008822	7.4	292.57	2.57626	0.002379
1.74	42.098	1.62426	0.023754	4.74	114.44	2.05856	0.008730	7.5	295.29	2.58226	0.002314
1.75	42.521	1.62860	0.023518	4.75	115.58	2.06290	0.008639	7.6	298.03	2.58826	0.002249
1.76	42.948	1.63295	0.023284	4.76	116.75	2.06724	0.008548	7.7	300.79	2.59426	0.002184
1.77	43.380	1.63729	0.023052	4.77	117.93	2.07158	0.008456	7.8	303.57	2.60026	0.002119
1.78	43.816	1.64163	0.022823	4.78	119.10	2.07593	0.008365	7.9	306.37	2.60626	0.002054
1.79	44.256	1.64598	0.022596	4.79	120.30	2.08027	0.008273	8.0	309.19	2.61226	0.001989
1.80	44.701	1.65032	0.022371	4.80	121.51	2.08461	0.008182	8.1	312.03	2.61826	0.001924
1.81	45.150	1.65466	0.022149	4.81	122.75	2.08895	0.008091	8.2	314.89	2.62426	0.001859
1.82	45.604	1.65900	0.021928	4.82	123.97	2.09329	0.008001	8.3	317.77	2.63026	0.001794
1.83	46.063	1.66335	0.021710	4.83	125.21	2.09763	0.007910	8.4	320.67	2.63626	0.001729
1.84	46.526	1.66769	0.021494	4.84	126.47	2.10197	0.007820	8.5	323.59	2.64226	0.001664
1.85	46.993	1.67203	0.021280	4.85	127.74	2.10631	0.007730	8.6	326.53	2.64826	0.001599
1.86	47.465	1.67638	0.021068	4.86	129.02	2.11065	0.007640	8.7	329.49	2.65426	0.001534
1.87	47.942	1.68072	0.020858	4.87	130.32	2.11500	0.007550	8.8	332.47	2.66	

Reciprocals' of the Integers 1-999

Reciprocal of $n = 1/n$

n	0	1	2	3	4	5	6	7	8	9
0		1.00000000	0.50000000	0.33333333	0.25000000	0.20000000	0.16666667	0.14285714	0.12500000	0.11111111
10	0.10000000	0.90909090	0.45454545	0.33333333	0.25000000	0.20000000	0.16666667	0.14285714	0.12500000	0.11111111
20	0.05000000	0.47619047	0.23809523	0.16666667	0.12500000	0.10000000	0.08333333	0.07142857	0.06250000	0.05555556
30	0.03333333	0.32258064	0.16666667	0.11111111	0.08333333	0.06666667	0.05555556	0.04761904	0.04166667	0.03703703
40	0.02500000	0.24390243	0.12500000	0.08333333	0.06250000	0.05000000	0.04166667	0.03571428	0.03125000	0.02777778
50	0.02000000	0.19607843	0.10000000	0.06666667	0.05000000	0.04000000	0.03333333	0.02857142	0.02500000	0.02222222
60	0.16666667	16393444	16129033	15873022	15625000	15384621	15151515	14925373	14705882	14492727
70	14285714	10484511	13688889	13485111	13333333	13157894	12987013	12825000	12671929	12526882
80	12500000	12345678	12195121	12048191	11904761	11763717	11625000	11489583	11356364	11225296
90	11111111	10989011	10869577	10752691	10638300	10526312	10416667	10309288	10204068	10101010
100	0.01000000	0.00990099	0.00980392	0.00970878	0.00961538	0.00952381	0.00943396	0.00934579	0.00925929	0.00917431
110	0.00909090	0.00900909	0.00892857	0.00884958	0.00877193	0.00869562	0.00862069	0.00854700	0.00847456	0.00840336
120	0.00833333	0.00826446	0.00819721	0.00813181	0.00806816	0.00800600	0.00794538	0.00788625	0.00782857	0.00777232
130	0.00769230	0.00763588	0.00757958	0.00752439	0.00747027	0.00741721	0.00736521	0.00731425	0.00726433	0.00721544
140	0.00714285	0.00709219	0.00704225	0.00699307	0.00694464	0.00689695	0.00685000	0.00680378	0.00675829	0.00671354
150	0.00666667	0.00662517	0.00658477	0.00654548	0.00650721	0.00646996	0.00643373	0.00639851	0.00636429	0.00633107
160	0.00625000	0.00621180	0.00617480	0.00613896	0.00610427	0.00607073	0.00603834	0.00600700	0.00597671	0.00594747
170	0.00588235	0.00584793	0.00581463	0.00578242	0.00575130	0.00572127	0.00569233	0.00566448	0.00563772	0.00561205
180	0.00555556	0.00552486	0.00549505	0.00546613	0.00543809	0.00541094	0.00538468	0.00535921	0.00533462	0.00531091
190	0.00526315	0.00523562	0.00520933	0.00518427	0.00516043	0.00513780	0.00511538	0.00509416	0.00507414	0.00505532
200	0.00500000	0.00497512	0.00495045	0.00492610	0.00490206	0.00487834	0.00485493	0.00483183	0.00480903	0.00478653
210	0.00476190	0.00473936	0.00471701	0.00469486	0.00467291	0.00465116	0.00462961	0.00460826	0.00458711	0.00456616
220	0.00454545	0.00452487	0.00450450	0.00448430	0.00446426	0.00444438	0.00442465	0.00440507	0.00438564	0.00436635
230	0.00434782	0.00432904	0.00431045	0.00429204	0.00427381	0.00425574	0.00423783	0.00421997	0.00420226	0.00418470
240	0.00416667	0.00414938	0.00413231	0.00411546	0.00409881	0.00408236	0.00406611	0.00405005	0.00403418	0.00401849
250	0.00400000	0.00398406	0.00396825	0.00395256	0.00393700	0.00392156	0.00390625	0.00389105	0.00387596	0.00386100
260	0.00384615	0.00383148	0.00381694	0.00380251	0.00378819	0.00377397	0.00375986	0.00374585	0.00373194	0.00371812
270	0.00370370	0.00369037	0.00367717	0.00366409	0.00365112	0.00363826	0.00362551	0.00361286	0.00360031	0.00358786
280	0.00357142	0.00355879	0.00354630	0.00353394	0.00352170	0.00350957	0.00349754	0.00348561	0.00347378	0.00346204
290	0.00348276	0.00347062	0.00345864	0.00344681	0.00343512	0.00342357	0.00341215	0.00340086	0.00338969	0.00337864
300	0.00333333	0.00332259	0.00331198	0.00330150	0.00329114	0.00328090	0.00327077	0.00326075	0.00325084	0.00324103
310	0.00322580	0.00321543	0.00320518	0.00319504	0.00318501	0.00317508	0.00316525	0.00315551	0.00314587	0.00313633
320	0.00312500	0.00311526	0.00310560	0.00309603	0.00308655	0.00307716	0.00306786	0.00305865	0.00304953	0.00304050
330	0.00303030	0.00302118	0.00301214	0.00300317	0.00299427	0.00298543	0.00297665	0.00296793	0.00295927	0.00295066
340	0.00294117	0.00293251	0.00292397	0.00291545	0.00290697	0.00289851	0.00289010	0.00288173	0.00287341	0.00286513
350	0.00285714	0.00284903	0.00284099	0.00283298	0.00282500	0.00281704	0.00280910	0.00280118	0.00279329	0.00278541
360	0.00277778	0.00277003	0.00276231	0.00275461	0.00274693	0.00273927	0.00273163	0.00272401	0.00271640	0.00270881
370	0.00270370	0.00269618	0.00268867	0.00268118	0.00267370	0.00266623	0.00265877	0.00265133	0.00264390	0.00263647
380	0.00263157	0.00262427	0.00261698	0.00260970	0.00260243	0.00259517	0.00258792	0.00258068	0.00257345	0.00256622
390	0.00256410	0.00255745	0.00255080	0.00254415	0.00253750	0.00253085	0.00252420	0.00251755	0.00251090	0.00250425
400	0.00250000	0.00249376	0.00248752	0.00248129	0.00247506	0.00246883	0.00246260	0.00245637	0.00245014	0.00244391
410	0.00243902	0.00243300	0.00242698	0.00242096	0.00241493	0.00240890	0.00240287	0.00239684	0.00239081	0.00238478
420	0.00238095	0.00237527	0.00236958	0.00236389	0.00235820	0.00235251	0.00234682	0.00234113	0.00233544	0.00232975
430	0.00232581	0.00232018	0.00231451	0.00230884	0.00230317	0.00229750	0.00229183	0.00228616	0.00228049	0.00227482
440	0.00227272	0.00226754	0.00226233	0.00225712	0.00225191	0.00224670	0.00224149	0.00223628	0.00223107	0.00222586
450	0.00222222	0.00221729	0.00221238	0.00220746	0.00220255	0.00219764	0.00219273	0.00218782	0.00218291	0.00217800
460	0.00217391	0.00216917	0.00216442	0.00215967	0.00215492	0.00215017	0.00214542	0.00214067	0.00213592	0.00213117
470	0.00212660	0.00212312	0.00211964	0.00211615	0.00211266	0.00210917	0.00210568	0.00210219	0.00209870	0.00209521
480	0.00208333	0.00208000	0.00207667	0.00207333	0.00206999	0.00206666	0.00206333	0.00205999	0.00205666	0.00205333
490	0.00204816	0.00204500	0.00204183	0.00203866	0.00203549	0.00203232	0.00202915	0.00202598	0.00202281	0.00201964
500	0.00200000	0.00199608	0.00199216	0.00198824	0.00198432	0.00198040	0.00197648	0.00197256	0.00196864	0.00196472
510	0.00196078	0.00195694	0.00195310	0.00194926	0.00194542	0.00194158	0.00193774	0.00193390	0.00193006	0.00192622
520	0.00192307	0.00191936	0.00191565	0.00191194	0.00190823	0.00190452	0.00190081	0.00189710	0.00189339	0.00188968
530	0.00188672	0.00188323	0.00187973	0.00187623	0.00187273	0.00186923	0.00186573	0.00186223	0.00185873	0.00185523
540	0.00185185	0.00184849	0.00184512	0.00184175	0.00183838	0.00183500	0.00183163	0.00182825	0.00182488	0.00182150
550	0.00181818	0.00181488	0.00181158	0.00180828	0.00180498	0.00180168	0.00179838	0.00179508	0.00179178	0.00178848
560	0.00178751	0.00178431	0.00178111	0.00177791	0.00177471	0.00177151	0.00176831	0.00176511	0.00176191	0.00175871
570	0.00175438	0.00175131	0.00174823	0.00174515	0.00174207	0.00173900	0.00173592	0.00173284	0.00172976	0.00172668
580	0.00174213	0.00173917	0.00173621	0.00173325	0.00173029	0.00172733	0.00172437	0.00172141	0.00171845	0.00171549
590	0.00169418	0.00169127	0.00168836	0.00168545	0.00168254	0.00167963	0.00167672	0.00167381	0.00167090	0.00166799
600	0.00166667	0.00166384	0.00166100	0.00165817	0.00165533	0.00165250	0.00164967	0.00164683	0.00164400	0.00164116
610	0.00163934	0.00163661	0.00163387	0.00163113	0.00162839	0.00162565	0.00162291	0.00162017	0.00161743	0.00161469
620	0.00161290	0.00161023	0.00160756	0.00160489	0.00160222	0.00159955	0.00159688	0.00159421	0.00159154	0.00158887
630	0.00158730	0.00158476	0.00158221	0.00157966	0.00157711	0.00157456	0.00157201	0.00156946	0.00156691	0.00156436
640	0.00156250	0.00156000	0.00155750	0.00155500	0.00155250	0.00155000	0.00154750	0.00154500	0.00154250	0.00154000
650	0.00153846	0.00153608	0.00153370	0.00153132	0.00152894	0.00152656	0.00152418	0.00152180	0.00151942	0.00151704
660	0.00151512	0.00151285	0.00151057	0.00150829	0.00150601	0.00150373	0.00150145	0.00149917	0.00149689	0.00149461
670	0.00149253	0.00149031	0.00148809	0.00148587	0.00148365	0.00148143	0.00147921	0.00147699	0.00147477	0.00147255
680	0.00147058	0.00146842	0.00146626	0.00146410	0.00146194	0.00145978	0.00145762	0.00145546	0.00145330	0.00145114
690	0.00144927	0.00144718	0.00144508	0.00144298	0.00144088	0.00143878	0.00143668	0.00143458	0.00143248	0.00143038
700	0.00142857	0.00142653	0.00142448	0.00142243	0.00142038	0.00141833	0.00141628	0.00141423	0.00141218	0.00141013
710	0.00140845	0.00140640	0.00140435	0.00140230	0.00140025	0.00139820	0.00139615	0.00139410	0.00139205	0.00139000
720	0.00138889	0.00138693	0.00138497	0.00138301	0.00138105	0.00137910	0.00137714	0.00137518	0.00137322	0.00137126
730	0.00136983	0.00136798	0.00136612	0.00136426	0.00136240	0.00136054	0.00135868	0.00135682	0.00135496	0.00135310
740	0.00135135	0.00134958	0.00134779	0.00134595	0.00134411	0.00134227	0.00134043	0.00133859	0.00133675	0.00133491
750	0.00133333	0.00133158								

n	0	1	2	3	4	5	6	7	8	9
0	0	1	8	27	64	125	216	343	512	729
10	1000	1331	1728	2167	2744	3375	4096	4913	5832	6859
20	8000	9261	10648	12167	13824	15625	17568	19663	21912	24327
30	27000	29791	32768	35937	39304	42875	46656	50653	54872	59319
40	64000	68021	72272	76857	81684	86761	92088	97665	103492	109579
50	125000	132651	140608	148877	157464	166375	175616	185193	195112	205379
60	216000	226981	238328	250047	262136	274601	287536	299947	312832	326199
70	343000	359121	375728	392817	410396	428471	447048	466133	485732	505859
80	512000	531441	551368	571787	592704	614125	636056	658503	681472	704969
90	729000	750261	771936	794031	816552	839605	863196	887331	911916	937059
100	1000000	1030301	1061208	1092727	1124864	1157635	1191048	1225113	1259742	1295049
110	1331000	1377631	1424028	1472187	1522116	1573831	1627348	1682673	1739812	1798789
120	1728000	1787361	1848848	1912487	1978296	2046281	2116456	2188827	2263492	2340459
130	2197000	2269361	2343968	2421827	2502956	2587361	2675048	2766023	2859392	2955259
140	2744000	2828221	2914896	3004131	3096932	3193305	3293248	3396767	3503868	3614569
150	3375000	3472951	3573808	3677577	3784264	3893885	4006548	4122261	4241032	4362869
160	4096000	4207281	4321528	4438747	4558936	4682101	4808248	4937383	5069512	5204749
170	4913000	5036221	5162448	5291687	5423944	5559225	5697548	5838919	5983344	6130829
180	5832000	5967241	6105488	6246847	6391326	6538931	6689672	6843557	6999592	7157789
190	6853000	6999721	7149968	7303727	7461006	7621811	7786160	7954069	8125544	8299699
200	8000000	8260301	8524048	8791257	9061936	9336191	9614040	9895499	10180572	10469269
210	9261000	9533981	9810928	10091937	10386606	10684941	10987048	11292933	11601602	11913159
220	10648000	10938661	11241048	11545167	11852016	12161691	12475200	12792649	13114144	13439689
230	12167000	12479361	12804048	13131167	13461726	13795731	14133190	14474119	14818524	15176509
240	13824000	14159361	14508048	14869167	15242726	15619731	16000190	16384119	16771524	17162509
250	15625000	15982951	16354048	16738287	17135676	17546211	17969900	18406849	18857064	19320549
260	17568000	17947981	18341048	18747287	19166706	19599311	20045120	20504149	20976404	21461889
270	19663000	19962361	20275048	20601167	20940726	21293731	21760190	22240119	22733524	23240509
280	21912000	22230361	22562048	22907167	23265726	23637731	24023190	24412119	24814524	25230509
290	24327000	24664721	25016048	25381167	25760026	26152731	26559290	26979719	27414124	27862509
300	27000000	27450301	27914048	28391287	28882026	29386361	29904300	30435949	30981304	31540469
310	29791000	30253661	30730048	31219287	31721426	32236561	32764690	33305919	33860344	34428969
320	32768000	33243361	33732048	34234167	34749726	35278731	35821190	36377219	36946924	37530309
330	35937000	36425361	36927048	37442167	37970726	38512731	39068190	39637219	40219924	40816309
340	39304000	39803661	40316048	40842167	41381026	41932731	42497390	43075019	43665724	44269509
350	42875000	43387361	43913048	44452167	44904726	45470731	46050190	46643219	47249924	47860309
360	46656000	47180361	47718048	48269167	48833726	49401731	49983190	50578219	51186924	51809309
370	50653000	51189361	51739048	52292167	52858726	53438731	54032190	54639219	55259924	55894309
380	54872000	55429361	56000048	56584167	57181726	57792731	58417190	59055219	59706924	60372309
390	59319000	59897661	60490048	61096167	61715726	62348731	62995190	63655219	64328924	65016309
400	64000000	64603361	65221048	65853167	66499726	67160731	67836190	68526219	69230924	69950309
410	68921000	69546361	70185048	70838167	71505726	72187731	72984190	73795219	74620924	75461309
420	74058000	74704361	75364048	76038167	76726726	77430731	78150190	78885219	79635924	80402309
430	79307000	80006361	80720048	81449167	82193726	82953731	83729190	84520219	85326924	86149309
440	83734000	84453361	85187048	85935167	86697726	87474731	88266190	89072219	89893924	90731309
450	91219000	91958361	92712048	93480167	94262726	95060731	95874190	96703219	97547924	98408309
460	93766000	94525361	95299048	96087167	96899726	97736731	98588190	99453219	100331924	101125309
470	103823000	10463361	10545048	10628367	10713326	10800931	10891190	109840219	110786324	111749309
480	105952000	10678361	10762648	10848167	10935826	11025631	11117590	112117219	113080324	114054309
490	116469000	11733361	11821048	11910867	12002926	12097231	12193690	122923219	123931324	124951309
500	126500000	12748361	12848048	12949167	13051726	13155731	13261190	133681219	134766324	135867309
510	132500000	13359361	13470048	13582167	13695726	13810731	13927190	140451219	141645324	142855309
520	142500000	14369361	14490048	14612167	14735726	14860731	14987190	151151219	152445324	153755309
530	152500000	15379361	15510048	15642167	15775726	15910731	16047190	161851219	163245324	164655309
540	162500000	16389361	16530048	16672167	16815726	16960731	17107190	172551219	174045324	175555309
550	166373000	16786361	16937048	17089167	17242726	17397931	17554690	177129219	178726324	180338309
560	173161000	17475361	17636048	17798167	17961726	18126931	18293690	184620219	186319324	188034309
570	183193000	18489361	18661048	18834167	19008726	19184931	19362690	195420219	197229324	199054309
580	191171000	19298361	19481048	19665167	19850726	20037931	20226690	204170219	206090324	208026309
590	203797000	20572361	20767048	20963167	21160726	21360731	21563190	217672219	219729324	221802309
600	216600000	21864361	21970048	22177167	22385726	22595731	22807190	230202219	232348324	234509309
610	226190000	22833361	22949048	23166167	23384726	23604731	23826190	240492219	242739324	245002309
620	238320000	24056361	24282048	24509167	24737726	24967731	25199190	254322219	256669324	259032309
630	250470000	25281361	25517048	25754167	25992726	26232731	26474190	267172219	269619324	272082309
640	262640000	26508361	26754048	27001167	27249726	27500731	27753190	280072219	282629324	285202309
650	274850000	27739361	27995048	28252167	28510726	28771731	29035190	293002219	295669324	298352309
660	287190000	28983361	29249048	29516167	29784726	30054731	30326190	305992219	308739324	311502309
670	300000000	30274361	30550048	30827167	31105726	31385731	31667190	319502219	322349324	325212309
680	313430000	31628361	31915048	32203167	32492726	32784731	33078190	333732219	336699324	339682309
690	327500000	33046361	33344048	33643167	33943726	34245731	34549190	348542219	351609324	354692309
700	342200000	34526361	34834048	35143167	35453726	35765731	36079190	363942219	367109324	370292309
710	357530000	36069361	36387048	36706167	37026726	37348731	37672190	379972219	383239324	386522309
720	373500000	37676361	37994048	38313167	38632726	38953731	39276190	395992219	399239324	402502309
730	389170000	39253361	39591048	39930167	40270726	40612731	40956190	413012219	416479324	420062309
740	405520000	40898361	41246048	41595167	41945726	42297731	42651190	430062219	433629324	437212309
750	422570000	42613361	42971048	43330167	43690726	44052731	44416190	447812219	451479324	455162309
760	440320000	44398361	44766048	45135167	45505726	45877731	46251190	466262219	470029324	473812309
770	458770000	46243361	46611048	46980167	47350726	47722731	48096190	484712219	488479324	492262309
780	477920000	48158361	48526048	48895167	49265726	49637731	50011190	503862219	507629324	511412309
790	497770000	50143361	50511048	50879167	51248726	51619731	51992190	523652219	527399324	531162309
800	518320000	52198361	52566048	52935167	53305726	53677731	54051190	544262219	548029324	551812309
810	539570000	54323361	54691048	55060167	55430726	55802731	56176190	565512219	569279324	573062309
820	561520000	56518361	56886048	57255167	57625726	58007731	58391190	587762219	591629324	595512309
830	584270000	58793361	59161048	59530167	59900726	60272731	60646190	610212219	613979324	617762309
840	607820000	61148361	61516048	61885167	62255726	62627731	63001190	633762219	637529324	641312309
850	632170000	63583361	63951048	64320167	64690726	65062731	65436190	658112219	661879324	665662309
860	657420000	66108361	66476048	66845167	67215726	67587731	67961190	683362219	687129324	690912309
870	68347									

I. Symbols

$a \rightarrow b$	a tending toward b
∞	Infinity
\lim	Limiting value
$\sim b$	a approximately equal to b
$\approx b$	a very nearly equal to b
$= b$	a equal to b [cf. (1) below]
$\equiv b$	a identical with b (for formulae only)
$> b$	a greater than b
$< b$	a smaller than b
$\gg b$	a much greater than b
$\ll b$	a much smaller than b
$\neq b$	a not equal to b
$\leq b$	a equal to or smaller than b , i.e., a at most as great as b
$< a < c$	a greater than b and smaller than c
$\geq b$	a equal to or greater than b , i.e., a at least as great as b
$\leq b$	a equal to or smaller than b , i.e., a at most as great as b
$\leq a \leq c$	a lying between b and c
$ a $	Absolute value of a ; this is always positive, for example $ -5 = 5$
$+$	Addition sign, plus, positive
$-$	Subtraction sign, minus, negative
\cdot or \times	Multiplication sign, times (the period sign is not used in these <i>Tables</i>)
\div	Division sign, divided by (the sign \div is not used in these <i>Tables</i>)
$+b=c$	$a+b$, read as 'a plus b', denotes the sum of a and b . The result of the addition, c , is also known as the sum
$\sum_{i=1}^n x_i$	Sum of all values x_1, x_2, x_3, \dots , i.e., of all values x_i , from $i=1$ to $i=n$ inclusive, or $\sum_{i=1}^n x_i = x_1 + x_2 + x_3 + \dots + x_n$ (the limits of the summation above and below the sign Σ are usually omitted if there is no possibility of confusion)
\int	Indefinite integral
\int_a^b	Definite integral, or integral between $x=a$ and $x=b$
$-b=c$	$a-b$, read as 'a minus b', denotes subtraction of b from a . a is the minuend, b the subtrahend; $a-b$, or c , is the difference. Subtraction is the opposite of addition
$\times b=c$	$a \times b$, read as 'a times b', denotes multiplication of a by b . a and b are the multiplicands or factors; $a \times b$, or c , is the product. For the sake of clarity the period sign is not used in these <i>Tables</i>
$b=c$	$a:b$, read as 'a divided by b', denotes division. a is the dividend, b the divisor; $a:b$, or c , is the quotient. Division is the opposite of multiplication and can also be represented by the fraction $\frac{a}{b}$ or a/b
a^b	a^b , read as 'a to the power b', is known as involution. a is the base, b the exponent; a^b , or c , is the b th power of a . In the special case of $a^2=c$, a^3 or c is the square of a ; in that of $a^3=c$, a^3 or c is the cube of a

$\sqrt[b]{a} = c$ $\sqrt[b]{a}$, is the b th root of a , b being known as the exponent. In the special case of $\sqrt[a]{a} = c$, $\sqrt[a]{a}$ or \sqrt{a} is known as the square root of a , and the root exponent is usually omitted, i.e., $\sqrt{a} = \sqrt[a]{a}$. In the special case of $\sqrt[a]{a} = c$, $\sqrt[a]{a}$ or c is known as the cube root of a . Extraction of a root is the opposite of involution. See also 'Logarithms', page 134

\log, \ln	See 'Logarithms', page 134
e	Base of natural (napierian) logarithms = 2.7182818284...
π	Ratio of the circumference of a circle to its diameter = 3.1415926535...
\sin	See page 138
\cos	
\tan, tg	
\arcsin	See page 139

II. Numbers

The *natural numbers* consist of all positive whole numbers (positive integers). Zero* and negative numbers are not natural numbers.

The *rational numbers* consist of all positive and negative integers and the fractions formed from them, and zero.

The *irrational numbers* are incommensurable quantities that cannot be expressed as quotients either of integers or of rational fractions. Examples are $\sqrt{2}$ and $\sqrt{5}$. π and e are also irrational numbers.

The *real numbers* consist of all rational and irrational numbers. The fundamental laws of real numbers are the following:

1. The four fundamental operations

Addition, subtraction, multiplication and division (except division by zero) can always and without ambiguity be carried out with real numbers.

2. The order of numbers

Between any two real numbers a and b there can exist only one of the three relationships

$$a = b \quad \text{or} \quad a > b \quad \text{or} \quad a < b$$

where

$$a = b \quad \text{when} \quad a - b = 0 \quad (1)$$

$$a > b \quad \text{when} \quad a - b > 0 \quad (2)$$

$$a < b \quad \text{when} \quad a - b < 0 \quad (3)$$

Examples of inequalities (2) and (3) are

$$\dots > 10 > 9 > \dots > 1 > 0 > -1 > \dots > -10 > \dots$$

$$\dots < -10 < -9 < \dots < -1 < 0 < 1 < \dots < 10 < \dots$$

3. The commutative law

$$a + b = b + a \quad (4)$$

$$ab = ba \quad (5)$$

4. The associative law

$$(a + b) + c = a + (b + c) \quad (6)$$

$$(ab)c = a(bc) \quad (7)$$

5. The distributive law

$$a(b + c) = ab + ac \quad (8)$$

III. Calculations with zero and infinity

$$a - a = 0 \quad (9)$$

$$0 = 0 \quad (10)$$

$$0 \times a = 0 \quad (11)$$

* Some mathematicians regard zero also as a natural number.

$$\frac{a}{\infty} = 0 \quad (a \neq \infty) \quad (12)$$

$$\frac{0}{a} = 0 \quad (a \neq 0) \quad (13)$$

$$\frac{a}{0} \quad \text{not defined} \quad (14)$$

$$0^a = 0 \quad (a > 0) \quad (15)$$

$$a^0 = 1 \quad (a \neq 0) \quad (16)$$

$$\lim_{(a \rightarrow \infty)} a^n = \begin{cases} \infty & \text{for } a > 1 \\ 1 & \text{for } a = 1 \\ 0 & \text{for } -1 < a < 1 \text{ and } a \neq 0 \\ \text{nonconvergent} & \text{for } a \leq -1 \end{cases} \quad (17)$$

$$\log_e 0 = -\infty \quad (r > 1) \quad (18)$$

$$\log_e \infty = +\infty \quad (r > 1) \quad (19)$$

$$\log_e 1 = 0 \quad (20)$$

$$0! = 1 \quad (21)$$

$$\binom{n}{0} = 1 \quad (22)$$

IV. Addition, subtraction, multiplication, division

1. Algebraic signs

If a, b, c are positive numbers, then

$$a \pm b = a \mp (-b) \quad (23)$$

$$a(-b) = (-a)b = -(ab) = -c \quad (24)$$

$$(-a)(-b) = +ab = +c \quad (25)$$

$$\frac{-b}{a} = -\frac{b}{a} = -\frac{b}{-a} = -c \quad (26)$$

$$\frac{-b}{-a} = +\frac{b}{a} = +c \quad (27)$$

2. Brackets

$$a - b - c - d = a - (b + c + d) \quad (28)$$

$$\pm a \pm b \pm c \pm d \pm e = a (\pm b \pm c \pm d \pm e) \quad (29)$$

$$\pm a \pm b \pm c \pm d = \pm a (b + c + d) \quad (30)$$

3. Conversion of divisions into multiplications

$$\frac{b}{a} = \frac{1}{a} \times b \quad (31)$$

For values of $1/a$ for numbers from 1 to 999 see page 18. Equation (31) is particularly useful in mechanical calculation with a constant divisor.

4. Conversion of multiplications and divisions into additions

If b is an integer (or can be converted into an integer), then

$$\left. \begin{aligned} ab &= a + a + a + \dots \\ b &= \frac{1}{a} + \frac{1}{a} + \frac{1}{a} + \dots \end{aligned} \right\} b \text{ components} \quad (32)$$

Equation (32) is particularly useful in the mechanical tabulation of linear functions.

5. Fractions

$$\frac{a}{a} = 1 \quad (a \neq 0) \quad (33)$$

$$\frac{ma}{mb} = \frac{a}{b} \quad (m \neq 0) \quad (34)$$

$$\frac{a}{b} + \frac{c}{b} = \frac{a+c}{b} \quad (\text{can also be used from right to left}) \quad (35)$$

$$\frac{a}{b} + \frac{c}{d} = \frac{ad+bc}{bd} \quad (\text{can also be used from right to left}) \quad (36)$$

$$\frac{a}{b} \times \frac{c}{d} = \frac{a}{d} \times \frac{c}{b} = \frac{ac}{bd} \quad (37)$$

$$\frac{a}{b} \div \frac{c}{d} = \frac{a}{b} \times \frac{d}{c} = \frac{a}{c} \times \frac{d}{b} = \frac{a}{c} \div \frac{b}{d} \quad (38)$$

6. Proportions

The equation

$$a : b = c : d \quad (39)$$

read as ' a is to b as c is to d ', is known as a proportion. a and d are the extremes, b and c the means of the proportion. The product of the extremes equals the product of the means.

$$ad = bc \quad (40)$$

If a constant proportion is of the type expressed by

$$a : b = b : c \quad (41)$$

then in accordance with equation (39), $ac = b^2$, that is, $b = \sqrt{ac}$.

b is known as the mean proportional between a and c , or the geometric mean of a and c ; c is known as the third proportional to a and b .

A special case of proportions of type (40) is the so-called 'golden section' (extreme and mean ratio)

$$\left. \begin{aligned} \frac{a}{b} &= \frac{b}{a-b}, \text{ that is} \\ b &= \frac{a(\sqrt{5}-1)}{2} = 0.618034 a \quad \text{or} \quad \frac{a}{b} = 1.618034 \end{aligned} \right\} \quad (42)$$

Another special case is that of the so-called 'normal' format, expressed by

$$\left. \begin{aligned} \frac{a}{b} &= \frac{b}{a/2}, \text{ that is} \\ b &= a/\sqrt{2} = 0.707107 a \quad \text{or} \quad \frac{a}{b} = 1.414214 \end{aligned} \right\} \quad (43)$$

If the individual values of two related variables x, y are such that

$$\frac{y_1}{x_1} = \frac{y_2}{x_2} = \frac{y_3}{x_3} = \dots = k \quad (44)$$

then

$$y = kx \quad (45)$$

read as ' y is proportional to x in the ratio k '. k is known as the proportionality constant. As x increases, y increases in proportion when k is positive, decreases when k is negative. The graphical representation of a proportional relationship on rectangular coordinates results in a straight line, whence the expression linear relationship. On the other hand, a linear relationship between x and y does not necessarily mean that they are proportional to one another since there are many straight lines that do not correspond to equation (45). For example, $y = a + kx$ is not a proportional relationship between x and y . In this case ($y - a$) is proportional to x .

If the individual values of two related variables x, y are such that

$$\left. \begin{aligned} \frac{y_1}{1/x_1} &= \frac{y_2}{1/x_2} = \frac{y_3}{1/x_3} = \dots = k \\ \text{that is} \\ y_1 x_1 &= y_2 x_2 = y_3 x_3 = \dots = k \end{aligned} \right\} \quad (46)$$

then

$$y = \frac{k}{x} \quad (47)$$

read as ' y is inversely proportional to x in the ratio k '. The graphical representation of an inversely proportional relationship on rectangular coordinates results in a hyperbola. Such a relationship is therefore a nonlinear one.

V. Powers and roots

1. Powers with integral exponents

If a and b are any real numbers, m and r positive integers, then

$$0^m = 0 \quad (m > 0) \quad (48)$$

$$a^0 = 1 \quad (a \neq 0) \quad (16)$$

$$\lim_{(m \rightarrow \infty)} a^m = \begin{cases} \infty & \text{for } a > 1 \\ 1 & \text{for } a = 1 \\ 0 & \text{for } -1 < a < 1 \text{ and } a \neq 0 \\ \text{nonconvergent} & \text{for } a \leq -1 \end{cases} \quad (17)$$

$$a \times a \times a \times \cdots (m \text{ factors}) = a^m \quad (48)$$

$$\frac{1}{a} \times \frac{1}{a} \times \frac{1}{a} \times \cdots (m \text{ factors}) = \frac{1}{a^m} = a^{-m} \quad (a \neq 0) \quad (49)$$

$$a^m \times b^m = (ab)^m \quad (50)$$

$$\frac{a^m}{b^m} = \left(\frac{a}{b}\right)^m = a^m b^{-m} \quad (b \neq 0) \quad (51)$$

$$a^m \times a^r = a^{m+r} \quad (52)$$

$$\frac{a^m}{a^r} = a^m a^{-r} = a^{m-r} \quad (a \neq 0) \quad (53)$$

$$(a^m)^r = (a^r)^m = a^{mr} \quad (54)$$

Algebraic signs: If in equations (48) to (54) R is the resulting absolute value of the base, ϵ the absolute value of the power, $2m$ or $2m-1$ the resulting even or uneven exponent, then

$$(\pm R)^{2m} = +\epsilon \quad (55)$$

$$(\pm R)^{2m-1} = \pm \epsilon \quad (56)$$

2. Extraction of roots with integral exponents

If a and b are any real numbers, n and s positive integers but not zero, then

$$\sqrt[n]{a} = a^{\frac{1}{n}} \quad (57)$$

$$\frac{1}{\sqrt[n]{a}} = a^{-\frac{1}{n}} \quad (a \neq 0) \quad (58)$$

$$\sqrt[n]{ab} = \sqrt[n]{a} \sqrt[n]{b} = (ab)^{\frac{1}{n}} \quad (59)$$

$$\sqrt[n]{\frac{a}{b}} = \frac{\sqrt[n]{a}}{\sqrt[n]{b}} = \left(\frac{a}{b}\right)^{\frac{1}{n}} \quad (b \neq 0) \quad (60)$$

$$\sqrt[s]{\sqrt[n]{a}} = \sqrt[ns]{a} = a^{\frac{1}{ns}} \quad (61)$$

Algebraic signs: If in equations (57) to (61) R is the resulting absolute value of the base, ϵ the absolute value of the power, $2n$ or $2n-1$ the resulting even or uneven exponent, then

$$\sqrt[2n]{(+R)} = (+R)^{\frac{1}{2n}} = +\epsilon \quad (62)$$

$$\sqrt[2n]{(-R)} = (-R)^{\frac{1}{2n}} \quad \text{has no real solution} \quad (63)$$

$$\sqrt[2n-1]{(\pm R)} = (\pm R)^{\frac{1}{2n-1}} = \pm \epsilon \quad (64)$$

3. Mixed powers and roots

If a and b are any real numbers, m and r positive integers, k , n and s likewise positive integers but not zero, then

$$\sqrt[n]{a^m} = a^{\frac{m}{n}} \quad (65)$$

$$\frac{1}{\sqrt[n]{a^m}} = a^{-\frac{m}{n}} \quad (a \neq 0) \quad (66)$$

$$\sqrt[s]{\sqrt[n]{a^k}} = \sqrt[ns]{a^k} = a^{\frac{k}{ns}} \quad (67)$$

If in equation (67) a is negative it is important that all other necessary conversion operations on the exponent should be performed before reduction is carried out. If the resulting numerator in the exponent is even, then a negative a is made positive and reduction carried out.

$$\sqrt[n]{(ab)^m} = \sqrt[n]{a^m} \times \sqrt[n]{b^m} = (ab)^{\frac{m}{n}} \quad (68)$$

$$\frac{\sqrt[n]{a^m}}{\sqrt[n]{b^m}} = \sqrt[n]{\left(\frac{a}{b}\right)^m} = \left(\frac{a}{b}\right)^{\frac{m}{n}} \quad (b \neq 0) \quad (69)$$

$$\sqrt[n]{a} \times \sqrt[n]{a} = a^{\frac{1}{n} + \frac{1}{n}} = a^{\frac{n+s}{ns}} = \sqrt[n]{a^{n+s}} \quad (70)$$

$$\sqrt[n]{a^m} \times \sqrt[n]{a^r} = a^{\frac{m}{n} + \frac{r}{n}} = a^{\frac{m+r}{ns}} = \sqrt[n]{a^{m+r}} \quad (71)$$

$$\left(a^{\frac{m}{n}}\right)^{\frac{r}{s}} = \left(a^{\frac{r}{s}}\right)^{\frac{m}{n}} = a^{\frac{mr}{ns}} \quad (72)$$

Algebraic signs: If in equations (65) to (72) R is the resulting absolute value of the base, ϵ the absolute value of the power, $2m$, $2n$, or $2m-1$, $2n-1$ respectively the resulting even or uneven numerator and denominator of the exponent, then

$$\sqrt[2m]{(\pm R)^{2n}} = (\pm R)^{\frac{2m}{2n}} = (+R)^{\frac{2m}{2n}} = +\epsilon \quad (73)$$

(always to be used in any reduction of an exponent)

$$\sqrt[2m]{(+R)^{2n-1}} = (+R)^{\frac{2m-1}{2n}} = +\epsilon \quad (74)$$

$$\sqrt[2m]{(-R)^{2n-1}} = (-R)^{\frac{2m-1}{2n}} \quad \text{has no real solution} \quad (75)$$

$$\sqrt[2n-1]{(\pm R)^{2m}} = (\pm R)^{\frac{2m}{2n-1}} = +\epsilon \quad (76)$$

$$\sqrt[2n-1]{(\pm R)^{2m-1}} = (\pm R)^{\frac{2m-1}{2n-1}} = \pm \epsilon \quad (77)$$

VI. Logarithms

In accordance with the equation

$$a = \epsilon^{\log_{\epsilon} a} \quad (78)$$

(a = number or antilogarithm, ϵ = base, $\log_{\epsilon} a$ = logarithm of a to the base ϵ)

the logarithm of a to the base ϵ is defined as the exponent of the power of the base ϵ which equals the number a . The usual bases are 10 (common or briggsian logarithms) and $e = 2.7182818285$ (natural, napierian or hyperbolic logarithms). In these *Tables* the symbol \log is used for common logarithms and the symbol \ln for natural logarithms. The relation between the two is given by

$$\ln a = \frac{\log a}{\log e} = 2.3025850930 \log a = \ln 10 \times \log a \quad (79)$$

$$\log a = \frac{\ln a}{\ln 10} = 0.4342944819 \ln a = \log e \times \ln a \quad (80)$$

In general the relation is expressed by

$$\log_{\epsilon} a = \frac{\log_{10} a}{\log_{10} \epsilon} \quad (81)$$

Example: It is required to find the logarithm of 20 to the base 2. From equation (81)

$$\log_2 20 = \frac{\log_{10} 20}{\log_{10} 2} = \frac{1.3010300}{0.3010300} = 4.321928$$

The use of logarithms reduces multiplication, division, raising to powers and the extraction of roots to addition, subtraction, multiplication and division respectively.

For common logarithms equation (78) gives

$$a = 10^{\log a} \quad \text{and} \quad b = 10^{\log b}$$

so that according to equation (52)

$$a \times b = 10^{\log a} \times 10^{\log b} = 10^{\log a + \log b}$$

$$\text{that is} \quad \log(a \times b) = \log a + \log b$$

$$\text{whence} \quad (a \times b) = \text{antilog}(\log a + \log b)$$

All the principles of logarithmic calculation can be deduced from section V in an analogous manner. The most important are:

$$\log(a \times b) = \log a + \log b \quad (82)$$

$$\log\left(\frac{a}{b}\right) = \log a - \log b \quad (83)$$

$$x^b = b \log x \quad (84)$$

$$\sqrt[b]{x} = \frac{\log x}{b} \quad (85)$$

By definition there are only logarithms of positive numbers. Logarithmic calculation is made without regard to the sign of a, b, \dots and the result assigned the appropriate sign according to the rules already given.

Logarithmic calculation falls into three parts:
 finding the logarithms
 operating with them according to the above rules
 finding the antilogarithms.

finding the logarithm

The number of which the logarithm is required is first converted into a product as follows:

$$= 10^k \times \frac{a}{10^m} = K' \times M' \quad (86)$$

determined for $|a| \geq 1$ by counting the number b of places to the left of the decimal point, for $|a| < 1$ by counting the number of places to the right of the decimal point, so that

$$= b - 1 \quad \text{when } |a| \geq 1 \quad (87)$$

$$= -b - 1 \quad \text{when } |a| < 1 \quad (88)$$

Examples

a	b	x	K'	$K' \times M'$
5663	4	3	10^4	$10^4 \times 1.5663$
12	1	0	10^1	$10^1 \times 1.2$
0.12	0	-1	10^{-1}	$10^{-1} \times 1.2$
0.00034	-3	-4	10^{-4}	$10^{-4} \times 3.4$

in accordance with equation (82)

$$\log a = \log(K' \times M') = \log K' + \log M' = K + M \quad (89)$$

is known as the characteristic, M as the mantissa of the logarithm of a .

For $M' < 1$, round off M' to 5 significant places
 For $M' \geq 1$, round off M' to 4 significant places

Example
 $\log 1.0993 \approx ? \quad \log 1.5663 \approx \log 1.566 = ?$

From the table on page 10

$\log 1.0993 = ? \quad \log 1.5663 \approx \log 1.566 = ?$

From the table on page 10

x	$\log x$	Proportional parts	
	6	7	3 6
109		0410	1 "
15	1931		

17

$$\log 1.0993 = 0.0410 + 0.0001 = 0.0411$$

$$\log 1.566 = 0.1931 + 0.0017 = 0.1948$$

Further examples

$$(a) \log 3048 = \log(10^3 \times 3.048) = 3 + 0.4829 + 0.0011 = 3.4840$$

$$(b) \log 0.2130 = \log(10^{-1} \times 2.130) = -1 + 0.3284 = -0.6716$$

$$(c) \log 1/3048 = \log(10^{-1} \times 3.048^{-1}) = -3 - (0.4829 + 0.0011) = -0.4840 - 3$$

$$(d) \log 1/0.2130 = \log(10^1 \times 2.130^{-1}) = 1 - 0.3284 = 0.6716$$

In example (c) the mantissa as well as the characteristic is negative. A negative mantissa must be converted into a positive one by adding 1 to the mantissa and subtracting 1 from the characteristic. For example:

$$-0.4840 - 3 = \underbrace{-0.4840 + 1}_{= 0.5160} \underbrace{- 3 - 1}_{= -4}$$

2. Operating with logarithms

This is done in accordance with equations (82) to (85) and the following rules:

1. To add or subtract logarithms, add or subtract the mantissas and the characteristics separately.

2. The mantissa x gives the number b of places to the left of the decimal point (when $x \geq 0$) or the number b of places to the right of the decimal point (when $x < 0$), as follows:

$$b = x + 1 \quad \text{when } x \geq 0 \quad (90)$$

$$b = -(x + 1) \quad \text{when } x < 0 \quad (91)$$

Examples

$$(a) \log(3048 \times 0.2130) = \begin{matrix} 3.4840 \\ + 0.3284 - 1 \\ \hline 3.8124 - 1 \end{matrix} = 2.8124$$

$$(b) \log(0.2130 \div 3048) = \begin{matrix} 0.3284 - 1 \\ + 0.5160 - 4 \\ \hline 0.8444 - 5 \end{matrix} = 0.8444 - 5$$

$$(c) \log(0.2130 \div 0.0003281) = \begin{matrix} 0.3284 - 1 \\ - 0.5160 - 4 \\ \hline 1.3284 - 2 \\ - 0.5160 + 4 \\ \hline 0.8124 + 2 \end{matrix} = 2.8124$$

$$(d) \log(0.2130^5) = 5 \log 0.2130 = 5 \times (0.3284 - 1) = 1.6420 - 5 = -0.6420 - 4$$

$$(e) \log(\sqrt[5]{0.2130}) = \frac{\log 0.2130}{5} = \frac{0.3284 - 1}{5} = \frac{5.3284 - 6}{5} = 0.8881 - 1$$

$$(f) \log(\sqrt[5]{0.2130}) = \frac{\log 0.2130}{1.5} = \frac{0.3284 - 1}{1.5} = \frac{0.8284 - 1.5}{1.5} = 0.5523 - 1$$

3. Finding the antilogarithm

The antilogarithm is found by means of equations (90) and (91).

determined by means of equations (90) and (91)

$$\text{Examples: antilog } 2.8124 = 647.2$$

$$\text{antilog } (0.8881 - 1) = 0.7729$$

$$\text{antilog } (0.6420 - 4) = 0.0004385$$

VII. Factorials and binomial coefficients

1. n^{th}

For a positive integer r and any real number n the symbol $n^{(r)}$ represents the product

$$n^{(r)} = n(n-1)(n-2) \cdots (n-r+1) \quad (92)$$

where

$$n^{(0)} = 1 \quad (93)$$

Examples:

$$(a) 10^{(4)} = ?$$

In this case, $(n - r + 1) = 10 - 4 + 1 = 7$, so that $10^{(4)} = 10 \times 9 \times 8 \times 7 = 5040$

$$(b) 4^{(4)} = ?$$

In this case, $(n - r + 1) = 4 - 5 + 1 = 0$, so that $4^{(4)} = 4 \times 3 \times 2 \times 1 \times 0 = 0$

From example (b) it can be seen that

$$n^{(r)} = 0 \quad (94)$$

when $r > n$ and n is a positive integer.

2. Factorials

The factorial of a positive integer n , symbol $n!$, is defined as

$$n! = n(n-1)(n-2) \cdots 3 \times 2 \times 1 \quad (95)$$

where

$$0! = 1 \quad (96)$$

by definition.

For positive integers n , the factorial $n!$ can be expressed as $n^{(n)}$, in which case equation (92) can be written

$$n^{(r)} = \frac{n!}{(n-r)!} \quad (97)$$

Equations (93) and (94) remain valid.

Logarithms of the factorials of numbers n from 1 to 999 and of their reciprocals are given on pages 26 and 27. For the factorials of numbers $n \geq 1000$ the STIRLING approximation is used:

$$\frac{n!}{(n \rightarrow \infty)} \rightarrow n^n e^{-n} \sqrt{2\pi n} \quad (98)$$

or

$$\log n! \rightarrow 0.5 \times [2n(\log n - 0.4342944819) + \log n + 0.798178] \quad (99)$$

3. Binomial coefficients

In its general form the binomial coefficient $\binom{n}{r}$ or $C(n, r)$ is defined as

$$\binom{n}{r} = \frac{n^{(r)}}{r!} \quad (100)$$

For $n^{(r)}$ and $r!$ see subsections 1 and 2 above.

When n is a positive integer equations (97) and (100) give

$$\binom{n}{r} = \frac{n!}{r!(n-r)!} \quad (101)$$

From equations (93), (94) and (96) it follows that

$$\binom{n}{0} = 1 \quad (102)$$

$$\binom{0}{0} = 1 \quad (103)$$

$$\binom{n}{r} = 0 \quad \text{when } r > n \text{ and } n \text{ is a positive integer.} \quad (104)$$

It is also clear that

$$\binom{n}{n} = 1 \quad (105)$$

Example: For $n = 9$ and $n = 10$ all the coefficients for values of r between zero and n are tabulated:

	r	0	1	2	3	4	$\frac{n}{2}$	5	6	7	8	9	
$n = 9$		1	9	36	84	126	126	84	36	9	1		
$n = 10$		1	10	45	120	210	252	210	120	45	10	1	
	r	0	1	2	3	4	$\frac{n}{2}$	5	6	7	8	9	10

It will be seen that as r increases, the values of $\binom{n}{r}$ increase up to $n/2$ and then decrease again in symmetrical fashion:

$$\binom{n}{r} = \binom{n}{n-r} \quad (106)$$

For uneven numbers n , the median falls between the two highest values of the series, for even numbers n it is at the highest value.

Binomial coefficients for n from zero to 39 and for r from zero to 15 are given on page 25. Logarithms of the binomial coefficients for n from 2 to 100 and for r from zero to $n/2$ are given on pages 70-77. For $101 \leq n \leq 999$ the binomial coefficients are calculated from equation (101) using the logarithms of factorials and their reciprocals given on pages 26 and 27.

VIII. Series

The sum $a_1 + a_2 + a_3 + \cdots + a_n$ of a sequence of numbers $a_1, a_2, a_3, \dots, a_n$ formed according to some fixed rule or law is known as a series.

1. Arithmetic series of the 1st order

This is a series in which the difference d between successive terms is constant:

$$a_2 - a_1 = a_3 - a_2$$

The individual terms are therefore

$$\left. \begin{array}{ccccccc} a_1 & a_2 & a_3 & \cdots & a_n \\ a_1 & (a_1 + d) & (a_1 + 2d) & \cdots & a_1 + (n-1)d \end{array} \right\} \quad (107)$$

The sum of the first n terms is

$$S = \frac{n(a_1 + a_n)}{2} \quad (108)$$

A special case of (108) is the sum of the natural sequence of numbers 1, 2, 3, ..., n

$$1 + 2 + 3 + \cdots + n = \frac{n(n+1)}{2} \quad (109)$$

Example: The sum of all numbers from 1 to 81 is

$$(81 \times 82) / 2 = 3321$$

2. Geometric series

A geometric series is one in which there is a constant ratio q between successive terms

$$\left. \begin{array}{ccccccc} a_1 & a_2 & a_3 & \cdots & a_n \\ a_1 & a_1 q & a_1 q^2 & \cdots & a_1 q^{n-1} \end{array} \right\} \quad (110)$$

The sum of the first n terms is

$$S = a_1 \frac{1 - q^n}{1 - q} = a_1 \frac{q^n - 1}{q - 1} \quad (q \neq 1) \quad (111)$$

When $-1 < q < 1$, $q^\infty = 0$ in accordance with (17), and (111) becomes

$$S_\infty = \frac{a_1}{1 - q} \quad (-1 < q < 1) \quad (112)$$

With the aid of equation (112) infinite periodic decimal fractions, for example, can be converted into true fractions.

Examples:

$$(a) 0.3333\bar{3} = \frac{3}{10} + \frac{3}{100} + \frac{3}{1000} + \cdots$$

$$q = \frac{1}{10} \quad a_1 = \frac{3}{10}$$

$$0.3333\bar{3} = \frac{3}{10} / \frac{9}{10} = \frac{3}{9} = \frac{1}{3}$$

$$(b) 0.0333\bar{3} = \frac{3}{100} + \frac{3}{1000} + \cdots$$

$$q = \frac{1}{10} \quad a_1 = \frac{3}{100}$$

Mathematical Symbols, Definitions and Formulae

$$0.0333\bar{3} = \frac{3}{100} \div \frac{9}{10} = \frac{3}{90} = \frac{1}{30}$$

$$(c) 0.2333\bar{3} = \frac{2}{10} + \frac{3}{100} + \frac{3}{1000} + \dots$$

The infinite series begins with $3/100$, whence $q = 1/10$, $a_1 = 3/100$, as in the previous example. There remains $2/10$ to be added to it

$$0.2333\bar{3} = \frac{2}{10} + \frac{1}{30} = \frac{60 + 10}{300} = \frac{7}{30}$$

$$(d) 0.123123123\bar{1} = \frac{123}{1000} + \frac{123}{1000000} + \dots$$

$$q = \frac{1}{1000} \quad a_1 = \frac{123}{1000}$$

$$0.123123\bar{1} = \frac{123}{1000} \div \frac{999}{1000} = \frac{123}{999} = \frac{41}{333}$$

Binomial series for positive integers n

$$(a+b)^n = \binom{n}{0} a^n b^0 + \binom{n}{1} a^{n-1} b^1 + \binom{n}{2} a^{n-2} b^2 + \dots + \binom{n}{n} a^0 b^n \quad (113)$$

Algebraic signs: When b is negative, all terms in which the exponent of b is uneven are negative

Examples: $(a+b)^3 = a^3 + 3a^2b + 3ab^2 + b^3$ etc

$$(a+b)^3 = a^3 + 3a^2b + 3ab^2 + b^3 \text{ etc}$$

IX. Means

For n positive variates x_1, x_2, \dots, x_n

$$(a) \text{ the arithmetic mean } m_a = \frac{x_1 + x_2 + \dots + x_n}{n} = \frac{\sum_{i=1}^n x_i}{n} \quad (114)$$

$$(b) \text{ the geometric mean } m_g = \sqrt[n]{x_1 \times x_2 \times \dots \times x_n} \quad (115)$$

$$(c) \text{ the harmonic mean } m_h = 1 \div \frac{1}{n} \left(\frac{1}{x_1} + \frac{1}{x_2} + \dots + \frac{1}{x_n} \right) \quad (116)$$

When $n = 2$, then

$$m_a = \frac{x_1 + x_2}{2} \quad (117)$$

$$m_g = \sqrt{x_1 x_2} \quad (118)$$

$$m_h = \frac{2x_1 x_2}{x_1 + x_2} \quad (119)$$

$$\text{Cauchy's principle } m_a \geq m_g \geq m_h \quad (120)$$

where the equality signs are valid only when

$$x_1 = x_2 = \dots = x_n$$

X. Solutions of equations

Solutions of equations exist only when all the denominators differ from zero

Required is x

$$ax \pm b = 0, \quad x = \mp \frac{b}{a} \quad (121)$$

$$\frac{a}{x} \pm b = 0, \quad x = \mp \frac{a}{b} \quad (122)$$

1. Simplification of equations of higher degree

$$(ax \pm b)^n \pm c = 0, \quad x = \frac{\sqrt[n]{\mp c \mp b}}{a} \quad (123)$$

$$\sqrt[n]{ax \pm b} \pm c = 0, \quad x = \frac{(\mp c)^n \mp b}{a} \quad (124)$$

2. Equations of the first degree with two unknowns

x and y are required

$$a_1 x + b_1 y + c_1 = 0$$

$$a_2 x + b_2 y + c_2 = 0$$

$$x = \frac{b_1 c_2 - b_2 c_1}{a_1 b_2 - a_2 b_1}$$

$$y = -\frac{a_1 x + c_1}{b_1} = -\frac{a_2 x + c_2}{b_2}$$

3. Equations of the first degree with three unknowns

x, y, z are required

$$a_1 x + b_1 y + c_1 z + d_1 = 0$$

$$a_2 x + b_2 y + c_2 z + d_2 = 0$$

$$a_3 x + b_3 y + c_3 z + d_3 = 0$$

Let

$$A = c_1 a_2 - c_2 a_1$$

$$B = c_2 b_1 - c_1 b_2$$

$$C = c_3 a_1 - c_1 a_3$$

$$D = c_3 a_2 - c_2 a_3$$

$$E = c_3 b_2 - c_2 b_3$$

$$F = c_3 d_1 - c_1 d_3$$

then

$$x = \frac{BF - CE}{AE - BD}$$

$$y = -\frac{C + Ax}{B} = -\frac{F + Dx}{E}$$

$$z = -\frac{a_1 x + b_1 y + d_1}{c_1} = -\frac{a_2 x + b_2 y + d_2}{c_2} = -\frac{a_3 x + b_3 y + d_3}{c_3}$$

4. Quadratic equations with one unknown

$$ax^2 + bx + c = 0$$

$$x_{1,2} = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a} = \frac{-b}{2a} \pm \sqrt{\left(\frac{b}{2a}\right)^2 - \frac{c}{a}}$$

The magnitude $D = b^2 - 4ac$ is known as the discriminant equation. When

$D > 0$ there are two real solutions

$D = 0$ there is only one real solution

$D < 0$ there is no real solution

5. Exponential equations in common use

$$x = 1 - e^{-t}, \quad x = 1 - \text{antilog}(-0.4342944619t)$$

$$a = 1 - e^{-t}, \quad t = -2.3025850930 \log(1-a) \quad [0 \leq a \leq 1]$$

If in equation (127)

$$z = \frac{ax^b \pm c}{d}, \text{ then } \log x = \frac{\log\left(\frac{dz \mp c}{a}\right)}{b}$$

(when $b = 1$ the log sign disappears on both sides)

$$z = \frac{ax^b \pm c}{d}, \text{ then } x = \frac{\log\left(\frac{dz \mp c}{a}\right)}{\log b} \quad (b \neq 1)$$

$$z = \frac{d}{ax^b \pm c}, \text{ then } \log x = \frac{\log\left(\frac{d}{z \mp c}\right)}{b}$$

(when $b = 1$ the log sign disappears on both sides)

$$z = \frac{d}{ab^x \pm c}, \text{ then } x = \frac{\log \left(\frac{d/z \mp c}{a} \right)}{\log b} \quad (b \neq 1) \quad (133)$$

Equations (130) to (133) have no solution when

$$(d/z \mp c) < 0 \quad \text{or} \quad (d/z \mp c) < 0$$

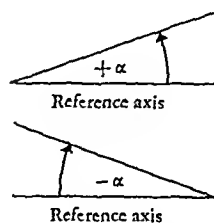
This is true for equations (130) and (132), however, only when $b \neq 1$.

The following table gives z values [solutions of equation (129)] for various numbers a in common use:

a	$1-a$	$\log(1-a)$	$z = -\ln 10 \times \log(1-a)$ $= -\ln(1-a)$
0.999	0.001	-3	6.907 755 279
0.995	0.005	0.698 970 004 3 -3	5.298 317 367
0.99	0.01	-2	4.605 170 186
0.975	0.025	0.397 940 008 7 -2	3.688 879 453
0.95	0.05	0.698 970 004 3 -2	2.995 732 274
0.90	0.10	-1	2.302 585 093
0.85	0.15	0.176 091 259 1 -1	1.897 119 985
0.80	0.20	0.301 029 995 7 -1	1.609 437 912
0.75	0.25	0.397 940 008 7 -1	1.386 294 361
0.70	0.30	0.477 121 254 7 -1	1.203 972 804
0.65	0.35	0.544 068 044 4 -1	1.049 822 124
0.60	0.40	0.602 059 991 3 -1	0.916 290 731 9
0.55	0.45	0.653 212 513 8 -1	0.798 507 696 2
0.50	0.50	0.698 970 004 3 -1	0.693 147 180 4
0.45	0.55	0.740 362 689 5 -1	0.597 837 000 7
0.40	0.60	0.778 151 250 4 -1	0.510 825 623 7
0.35	0.65	0.812 913 356 6 -1	0.430 782 916 2
0.30	0.70	0.845 098 040 0 -1	0.356 674 944 0
0.25	0.75	0.875 061 263 4 -1	0.287 682 072 4
0.20	0.80	0.903 089 987 0 -1	0.223 143 551 5
0.15	0.85	0.929 418 925 7 -1	0.162 518 929 5
0.10	0.90	0.954 242 509 4 -1	0.105 360 515 7
0.05	0.95	0.977 723 605 3 -1	0.051 293 294 39
0.025	0.975	0.989 004 615 7 -1	0.025 317 807 98
0.01	0.99	0.995 635 194 6 -1	0.010 050 335 85
0.005	0.995	0.997 823 080 7 -1	0.005 012 541 823
0.001	0.999	0.999 565 488 2 -1	0.001 000 500 333

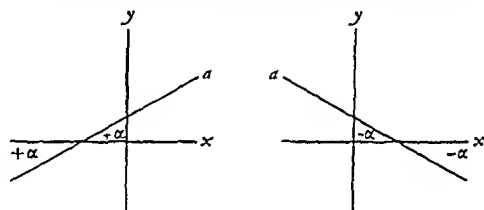
XII. Angles, trigonometric functions, inverse trigonometric functions

1. Positive and negative angles



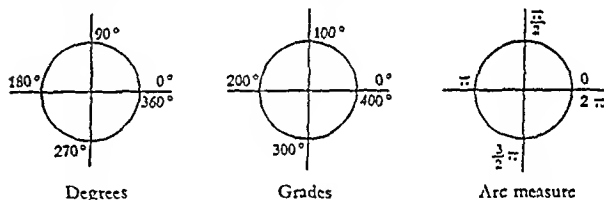
Rotation in an *anticlockwise* direction is defined as positive rotation, rotation in a clockwise direction as negative rotation. Similarly an angle measured by positive rotation is a positive angle, one measured by negative rotation a negative angle.

By angle of inclination of a straight line a is usually meant the *acute* angle between the straight line and the x axis.



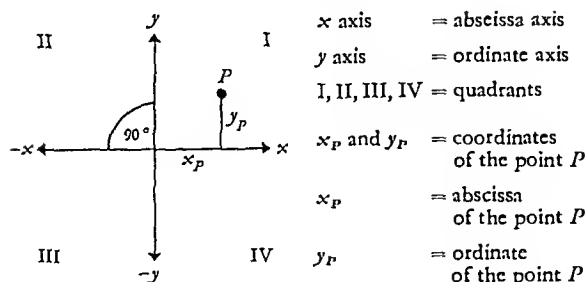
2. Angle units (see also under 'Units of Measurement', page 207)

The basis of all angle units is the circumference of a circle drawn with its centre at the point of intersection of the lines forming the angle. This is divided into 360 equal parts (degrees, the unit normally used) or into 400 equal parts (grades), or measured in terms of its own radius (arc, circular or radian measure). Since the circumference of a circle is 2π times its radius, angles are often expressed as fractions or multiples of π . The arc measure of the angle α is designated *arcus* α (arc α).



Degrees	0°	1°	30°	57°17'45"	60°	90°	180°	270°	360°
Arc measure	0	0.017 45	$\frac{\pi}{6}$	1	$\frac{\pi}{3}$	$\frac{\pi}{2}$	π	$\frac{3}{2}\pi$	2π

XI. Rectangular coordinate system



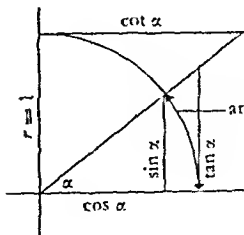
Signs of the coordinates of points in each of the 4 quadrants

Quadrant	x	y
I	+	+
II	-	+
III	-	-
IV	+	-

3. Trigonometric functions (other than secant and cosecant)

The definitions are based on the right triangle and are valid only for acute angles between 0 and 90°:

$$\left. \begin{aligned} \text{sine } \alpha &= \sin \alpha = \frac{a}{c} \\ \text{cosine } \alpha &= \cos \alpha = \frac{b}{c} \\ \text{tangent } \alpha &= \tan \alpha = \frac{a}{b} \\ \text{cotangent } \alpha &= \cot \alpha = \frac{b}{a} \end{aligned} \right\} \quad (134)$$



(the tangent is also sometimes abbreviated to tg, the cotangent to ctg or ctn)

Representation of trigonometric functions on the unit circle (circle with radius = 1)

Algebraic signs of trigonometric functions in the 4 quadrants

Function	Quadrant			
	I	II	III	IV
sin	+	+	-	-
cos	+	-	-	+
tan	+	-	+	-
cot	+	-	+	-

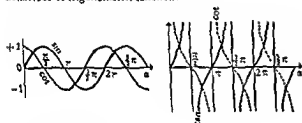
(135)

Ranges of trigonometric functions in the 4 quadrants

Function	Quadrant			
	I	II	III	IV
sin	0 to 1	1 to 0	0 to -1	-1 to 0
cos	1 to 0	0 to -1	-1 to 0	0 to 1
tan	0 to ∞	-∞ to 0	0 to ∞	-∞ to 0
cot	∞ to 0	0 to -∞	∞ to 0	0 to -∞

(134)

Behaviour of trigonometric functions



Functions of negative angles

$$\left. \begin{aligned} \sin(-\alpha) &= -\sin \alpha \\ \cos(-\alpha) &= +\cos \alpha \\ \tan(-\alpha) &= -\tan \alpha \\ \cot(-\alpha) &= -\cot \alpha \end{aligned} \right\} \quad (137)$$

Conversion of the functions of obtuse angles into those of acute angles

	$90^\circ \pm \alpha$	$180^\circ \pm \alpha$	$270^\circ \pm \alpha$	$\alpha^\circ (360^\circ) \pm \alpha$
sin	$+\cos \alpha$	$\mp \sin \alpha$	$-\cos \alpha$	$\pm \sin \alpha$
cos	$\mp \sin \alpha$	$-\cos \alpha$	$\pm \sin \alpha$	$+\cos \alpha$
tan	$\mp \cot \alpha$	$\pm \tan \alpha$	$\mp \cot \alpha$	$\pm \tan \alpha$
cot	$\mp \tan \alpha$	$\pm \cot \alpha$	$\mp \tan \alpha$	$\pm \cot \alpha$

(138)

* α = positive angleExample $\sin 125^\circ = \cos 35^\circ$

Relationships between trigonometric functions

Function	sin α	cos α	tan α	cot α
sin α	sin α	$\pm \sqrt{1 - \cos^2 \alpha}$	$\frac{\tan \alpha}{\pm \sqrt{1 + \tan^2 \alpha}}$	$\frac{1}{\pm \sqrt{1 + \cot^2 \alpha}}$
cos α	$\pm \sqrt{1 - \sin^2 \alpha}$	cos α	$\frac{1}{\pm \sqrt{1 + \tan^2 \alpha}}$	$\frac{\cot \alpha}{\pm \sqrt{1 + \cot^2 \alpha}}$
tan α	$\frac{\sin \alpha}{\pm \sqrt{1 - \sin^2 \alpha}}$	$\pm \frac{\sqrt{1 - \cos^2 \alpha}}{\cos \alpha}$	tan α	$\frac{1}{\cot \alpha}$
cot α	$\pm \frac{\sqrt{1 - \sin^2 \alpha}}{\sin \alpha}$	$\frac{\cos \alpha}{\pm \sqrt{1 - \cos^2 \alpha}}$	$\frac{1}{\tan \alpha}$	cot α

(139)

Algebraic signs of the square root. This is determined by the quadrant into which the angle falls. For algebraic signs in the quadrants see (135).

Functions of half the angle and of twice the angle

$$\left. \begin{aligned} \sin \frac{\alpha}{2} &= \pm \frac{1}{2} \left(\sqrt{1 + \sin \alpha} - \sqrt{1 - \sin \alpha} \right) \\ &= \pm \sqrt{\frac{1 - \cos \alpha}{2}} \end{aligned} \right\} \quad (140)$$

$$\cos \frac{\alpha}{2} = \pm \sqrt{\frac{1 + \cos \alpha}{2}} \quad (141)$$

$$\left. \begin{aligned} \tan \frac{\alpha}{2} &= \frac{1 - \cos \alpha}{\sin \alpha} = \frac{1 - \cos \alpha}{\sin \alpha} \\ &= \frac{\sin \alpha}{1 + \cos \alpha} = \pm \sqrt{\frac{1 - \cos \alpha}{1 + \cos \alpha}} \end{aligned} \right\} \quad (142)$$

$$\sin 2\alpha = 2 \sin \alpha \cos \alpha \quad (143)$$

$$\cos 2\alpha = 2 \cos^2 \alpha - 1 = 1 - 2 \sin^2 \alpha = \cos^2 \alpha - \sin^2 \alpha \quad (144)$$

$$\tan 2\alpha = \frac{2 \tan \alpha}{1 - \tan^2 \alpha} \quad (145)$$

Algebraic signs, \pm indicates that the algebraic sign is determined by the quadrant into which the required angle falls. For algebraic signs in the quadrants see (135).

Relationships between the functions of two angles

$$\sin(\alpha \pm \beta) = \sin \alpha \cos \beta \pm \cos \alpha \sin \beta \quad (146)$$

$$\cos(\alpha \pm \beta) = \cos \alpha \cos \beta \mp \sin \alpha \sin \beta \quad (147)$$

$$\tan(\alpha \pm \beta) = \frac{\tan \alpha \pm \tan \beta}{1 \mp \tan \alpha \tan \beta} = \frac{\sin(\alpha \pm \beta)}{\cos(\alpha \pm \beta)} \quad (148)$$

$$\sin \alpha + \sin \beta = 2 \sin \left(\frac{\alpha + \beta}{2} \right) \cos \left(\frac{\alpha - \beta}{2} \right) \quad (149)$$

$$\sin \alpha - \sin \beta = 2 \cos \left(\frac{\alpha + \beta}{2} \right) \sin \left(\frac{\alpha - \beta}{2} \right) \quad (150)$$

$$\cos \alpha + \cos \beta = 2 \cos \left(\frac{\alpha + \beta}{2} \right) \cos \left(\frac{\alpha - \beta}{2} \right) \quad (151)$$

$$\cos \alpha - \cos \beta = -2 \sin \left(\frac{\alpha + \beta}{2} \right) \sin \left(\frac{\alpha - \beta}{2} \right) \quad (152)$$

$$\tan \alpha \pm \tan \beta = \frac{\sin(\alpha \pm \beta)}{\cos \alpha \cos \beta} \quad (153)$$

$$\sin \alpha \sin \beta = \frac{1}{2} \cos(\alpha - \beta) - \frac{1}{2} \cos(\alpha + \beta) \quad (154)$$

$$\cos \alpha \cos \beta = \frac{1}{2} \cos(\alpha - \beta) + \frac{1}{2} \cos(\alpha + \beta) \quad (155)$$

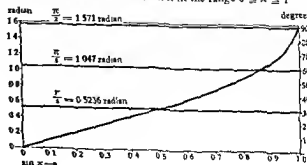
$$\sin \alpha \cos \beta = \frac{1}{2} \sin(\alpha + \beta) + \frac{1}{2} \sin(\alpha - \beta) \quad (156)$$

4. Inverse trigonometric functions

These are also known as arc or cyclometric functions. Only the inverse sine (arc-sine) function will be described here, since this is used for the stabilization of the variance of binomial distribution

(see page 187)

Arc sine x , abbreviated to $\sin^{-1} x$ or arc sin x , is the arc or degree measure of the angle with $\sin \alpha = x$. An arc sine table in arc measure for the range $0 \leq x \leq 1$ is given on page 65. If the value of an arc sine in degree is required, the value given in the table must be multiplied by $180/\pi = 57.295779513$.

Behaviour of the function arc sin x in the range $0 \leq x \leq 1$ 

XIII. Hyperbolic functions

These derive their name from their geometric representation in relation to a rectangular hyperbola in a manner similar to that in which the trigonometric functions are related to a circle. Here only the hyperbolic tangent ($\tanh z$) and the corresponding inverse function ($\tanh^{-1} r$) will be dealt with, since these functions are required for the transformation of the correlation coefficient r (see page 180). They are defined as follows:

$$\tanh z = r = \frac{e^{2z} - 1}{e^{2z} + 1}$$

(157)

$$\tanh^{-1} r = z = \frac{1}{2} \ln \frac{1+r}{1-r} = 1.151\,292\,55 \log_{10} \frac{1+r}{1-r}$$

(158)

Only the following two relationships are required:

$$\tanh(-z) = -\tanh z$$

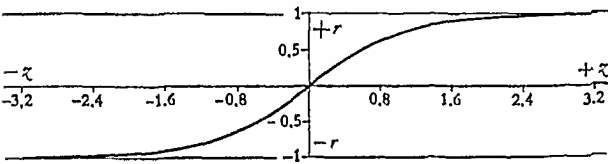
(159)

$$\tanh^{-1}(-r) = -\tanh^{-1} r$$

(160)

The range of variation of $\tanh z$ is -1 to $+1$ for values of z from $-\infty$ to $+\infty$.

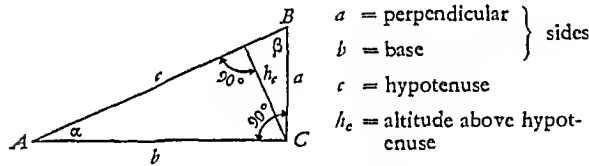
Behaviour of the function $\tanh z$ in the range $-3.2 \leq z \leq +3.2$



Tables of $\tanh z$ are given on pages 64 and 65, of $\tanh^{-1} r$ on page 62.

XIV. Geometric calculations

1. Right triangle ABC



- a = perpendicular

b = base

c = hypotenuse

h_c = altitude above hypot-
cuse

}

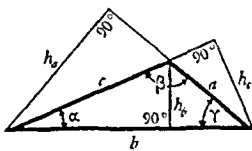
sides

Given	Required	Solution	
β	α	$= 90^\circ - \beta$	(161)
a, b	α	$\tan \alpha = \frac{a}{b}$	(162)
	c	$= \frac{a}{\sin \alpha}$	(163)
		$= \frac{b}{\cos \alpha}$	(164)
		$= \sqrt{a^2 + b^2}$	(165)
	h_c	$= a \cos \alpha$	(166)
		$= b \sin \alpha$	(167)
		$= \frac{ab}{c}$	(168)
	Area \mathcal{A}	$= \frac{ab}{2}$	(169)
a, c	α	$\sin \alpha = \frac{a}{c}$	(170)
	b	$= c \cos \alpha$	(171)
		$= \sqrt{c^2 - a^2}$	(172)

Given	Required	Solution	
a, c	Area \mathcal{A}	$= \frac{ac \cos \alpha}{2}$	(174)
b, c	α	$\cos \alpha = \frac{b}{c}$	(175)
	a	$= c \sin \alpha$	(176)
		$= \sqrt{c^2 - b^2}$	(177)
	h_c	$= b \sin \alpha$	(178)
	Area \mathcal{A}	$= \frac{bc \sin \alpha}{2}$	(179)
a, α	b	$= \frac{a}{\tan \alpha}$	(180)
	c	$= \frac{a}{\sin \alpha}$	(181)
	h_c	$= a \cos \alpha$	(182)
	Area \mathcal{A}	$= \frac{a^2}{2 \tan \alpha}$	(183)
c, α	a	$= c \sin \alpha$	(184)
	b	$= c \cos \alpha$	(185)
	h_c	$= \frac{c \sin 2\alpha}{2}$	(186)
	Area \mathcal{A}	$= \frac{c^2 \sin 2\alpha}{4}$	(187)
c, h_c	α	$\sin 2\alpha = \frac{2h_c}{c}$	(188)
	a	$= \frac{h_c}{\cos \alpha}$	(189)
	b	$= \frac{h_c}{\sin \alpha}$	(190)
	Area \mathcal{A}	$= \frac{c h_c}{2}$	(191)

2. Obtuse triangle

All the sides are of equal value in the obtuse triangle, and permutation of a, b, c , etc. in a cyclic fashion results in different formulae which are equally valid. When one of the symbols in any formula in a group is permuted, the symbols in all the other formulae of the group must be permuted in accordance with the following scheme:



Permutation by one step	Permutation by two steps	
$a \rightarrow b$	$a \rightarrow c$	(192)
$b \rightarrow c$	$b \rightarrow a$	
$c \rightarrow a$	$c \rightarrow b$	
$\alpha \rightarrow \beta$	$\alpha \rightarrow \gamma$	
$\beta \rightarrow \gamma$	$\beta \rightarrow \alpha$	
$\gamma \rightarrow \alpha$	$\gamma \rightarrow \beta$	

i areas	
$b \sin \gamma$	(193)
$c \sin \beta$	(194)
$a \frac{\sin \beta \sin \gamma}{\sin \alpha}$	(195)
$\frac{a h_a}{2}$	(196)

Required Solution

α	$= 180^\circ - (\beta + \gamma)$	(197)
$\sin (\beta + \gamma) = \sin \alpha$		(198)
$\cos (\beta + \gamma) = -\cos \alpha$		
$\tan (\beta + \gamma) = -\tan \alpha$		



$$\alpha \quad \cos \alpha = \frac{b^2 + c^2 - a^2}{2bc} \quad (199)$$

$$h_a = b \sin \gamma \quad (200)$$

$$= \frac{2A}{a} \quad (201)$$

$$\text{Area } A = \frac{bc \sin \alpha}{2} \quad (202)$$

$$= \frac{1}{2} r (r-a)(r-b)(r-c) \quad (203)$$

$$\text{where } r = \frac{a+b+c}{2}$$

$$\alpha \quad \tan \alpha = \frac{a \sin \gamma}{b - a \cos \gamma} \quad (204)$$



$$c = \frac{a \sin \gamma}{\sin \alpha} \quad (205)$$

$$= \sqrt{a^2 + b^2 - 2ab \cos \gamma} \quad (206)$$

$$h_a = b \sin \gamma \quad (207)$$

$$h_b = a \sin \gamma \quad (208)$$

$$\text{Area } A = \frac{a b \sin \gamma}{2} \quad (209)$$



$$\beta \quad \sin \beta = \frac{b \sin \alpha}{a} \quad (210)$$

$$c = \frac{a \sin \gamma}{\sin \alpha} \quad (211)$$

$$= b \cos \alpha \pm \sqrt{a^2 - b^2 \sin^2 \alpha} \quad (212)$$

$$h_a = b \sin \gamma \quad (213)$$

$$h_b = a \sin \gamma \quad (214)$$

$$h_c = b \sin \alpha \quad (215)$$

$$\text{Area } A = \frac{b}{2} \sin \alpha \times \left(b \cos \alpha \pm \sqrt{a^2 - b^2 \sin^2 \alpha} \right) \quad (216)$$



$$\alpha \quad \sin \alpha = \frac{a \sin \beta}{b} \quad (217)$$

$$c = \frac{b \sin \gamma}{\sin \beta} \quad (218)$$

$$h_a = b \sin \gamma \quad (219)$$

$$h_b = a \sin \gamma \quad (220)$$

Given Required Solution

$$a, b, \beta \quad h_a = a \sin \beta \quad (221)$$

$$\text{Area } A = \frac{a}{2} \sin \beta \gamma \quad (222)$$

$$\left\{ a \cos \beta \pm \sqrt{b^2 - a^2 \sin^2 \beta} \right\}$$

Note that in the above group of equations (given two sides and the angle they enclose), the following conditions hold:

$$\begin{array}{ll} \text{Equations} & \text{Equations} \\ (210) - (216) & (217) - (222) \end{array}$$

Solution is only possible when

$$b \sin \alpha \leq a \quad a \sin \beta \leq b$$

$$\text{If } b \sin \alpha = a \quad a \sin \beta = b$$

$$\text{then } \beta = 90^\circ \quad \alpha = 90^\circ$$

$$\text{If } b \sin \alpha < a \text{ and } a < b \quad a \sin \beta < b \text{ and } b < a$$

two solutions are possible

$$\beta_1 \text{ and } \beta_2 = 180^\circ - \beta_1 \quad \alpha_1 \text{ and } \alpha_2 = 180^\circ - \alpha_1$$

$$\text{If } b \sin \alpha < a \text{ and } a \geq b \quad a \sin \beta < a \text{ and } b \geq a$$

no solution is possible.

$$a, b, \gamma \quad b = \frac{a \sin \beta}{\sin (\beta + \gamma)} \quad (223)$$

$$c = \frac{a \sin \gamma}{\sin (\beta + \gamma)} \quad (224)$$

$$h_a = \frac{a \sin \beta \sin \gamma}{\sin (\beta + \gamma)} \quad (225)$$

$$h_b = a \sin \gamma \quad (226)$$

$$h_c = a \sin \beta \quad (227)$$

$$\text{Area } A = \frac{a^2}{2} \times \frac{\sin \beta \sin \gamma}{\sin (\beta + \gamma)} \quad (228)$$

$$\gamma = 180^\circ - (\alpha + \beta)$$

3 Quadrilateral

In general the area of any quadrilateral can be calculated from the diagonals and the angle θ (or $\theta' = 180^\circ - \theta$) enclosed by them.

Any quadrilateral

$$\sin \theta = \sin \theta' \quad \text{Area } A = \frac{2}{bc} \sqrt{r(r-a)(r-b)(r-c)} \quad (229)$$

where $s = \frac{1}{2}(a+b+c)$ is half the circumference of the triangle bounded by the two diagonals and the side a . Any triangle can be chosen, but the sides indicated by b, c must enclose the angle θ or θ' .

$$\text{Area of shaded part} = A \quad \text{Area } A = \frac{d_1 d_2 \sin \theta}{2} \quad (230)$$

Square

$$d = a\sqrt{2} = 1.414214 a \quad (231)$$

$$\text{Area } A = a^2 \quad (232)$$

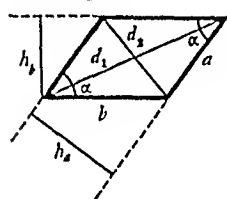
Rectangle

$$d = \sqrt{a^2 + b^2} \quad (233)$$

$$\text{Area } A = ab \quad (234)$$

$$$$

Parallelogram



$$d_1, d_2 = \sqrt{a^2 + b^2 \pm 2ab \cos \alpha} \quad (235)$$

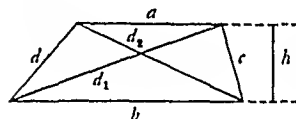
$$= \sqrt{a^2 + b^2 \pm 2a \sqrt{b^2 - h_a^2}} \quad (236)$$

$$h_a = b \sin \alpha \quad (237)$$

$$h_b = a \sin \alpha \quad (238)$$

$$\text{Area } A = ah_a = bh_b = ab \sin \alpha \quad (239)$$

Trapezoid



a, b are parallel, c, d nonparallel sides; d_1 = diagonal drawn between the points of intersection of d with b and a with c .

$$d_1 = \sqrt{ab + \frac{a^2 c^2 - b^2 d^2}{a - b}} \quad (240)$$

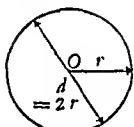
$$d_2 = \sqrt{ab + \frac{a^2 d^2 - b^2 c^2}{a - b}} \quad (241)$$

$$h = \frac{2}{a - b} \times \sqrt{s(s - a + b)(s - c)(s - d)} \quad (242)$$

where $s = \frac{1}{2}(a - b + c + d)$

$$\text{Area } A = \frac{(a + b)h}{2} \quad (243)$$

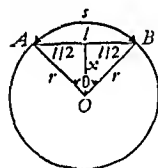
4. Circle



$$\left. \begin{aligned} \text{Circumference } c &= 2\pi r \\ &= 6.2831853r \\ &= 3.14159265d \end{aligned} \right\} \quad (244)$$

$$\left. \begin{aligned} \text{Area } A &= \pi r^2 = 3.14159265r^2 \\ &= 0.78539816d^2 \end{aligned} \right\} \quad (245)$$

Sector



Angle θ between the radii r

$$\cos \theta = 1 - \frac{l^2}{2r^2} \quad (246)$$

or

$$\theta = 180^\circ - 2 \arcsin(x/r) \quad (247)$$

Length of a chord

$$l = 2r \sin \frac{\theta}{2} \quad (248)$$

Length of an arc s

$$s = \frac{\pi r \theta}{180} = 0.017453293r\theta \quad (249)$$

Area of a sector

$$A_{se} = \frac{\pi r^2 \theta}{360} = 0.0087266463r^2 \theta \quad (250)$$

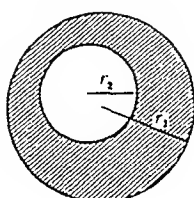
Area of a triangle OAB

$$A_{\Delta} = \frac{r^2 \sin \theta}{2} \quad (251)$$

Area of a segment Asp

$$\left. \begin{aligned} A_{sp} &= \frac{\pi r^2 \theta}{360} - \frac{r^2 \sin \theta}{2} \\ &= 0.0087266463r^2 \times \\ &\quad (0 - 57.2957795 \sin \theta) \end{aligned} \right\} \quad (252)$$

Annulus

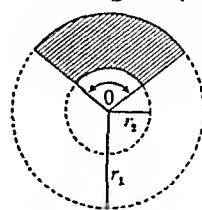


(The two circles bounding an annulus need not be concentric.)

Area of shaded part

$$\left. \begin{aligned} A &= \pi(r_1 + r_2)(r_1 - r_2) \quad [r_1 \geq r_2] \\ &= 3.14159265(r_1 + r_2)(r_1 - r_2) \end{aligned} \right\} \quad (253)$$

Annular segment (concentric)

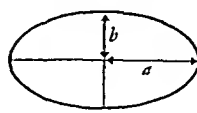


Area of shaded part

$$\left. \begin{aligned} A &= \frac{\pi \theta}{360} (r_1 + r_2)(r_1 - r_2) \quad [r_1 \geq r_2] \\ \frac{\pi}{360} &= 0.00872664626 \end{aligned} \right\} \quad (254)$$

For the angle θ see equations (246) and (247).

5. Ellipse

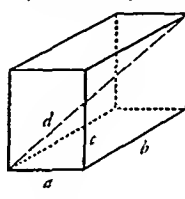


$$\left. \begin{aligned} \text{Circumference } c &\sim 2\pi \sqrt{\frac{a^2 + b^2}{2}} \\ &\sim 4.443 \sqrt{a^2 + b^2} \end{aligned} \right\} \quad (255)$$

$$\text{Area } A = \pi ab = 3.14159265ab \quad (256)$$

XV. Solid geometry

1. Rectangular parallelepiped (all edges at right angles to the adjacent ones)



Surface area

$$A = 2(ab + bc + ca) \quad (257)$$

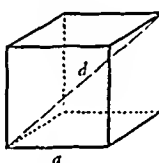
Internal diagonal

$$d = \sqrt{a^2 + b^2 + c^2} \quad (258)$$

Volume

$$V = abc \quad (259)$$

In the case of the cube, equations (257) to (259) become

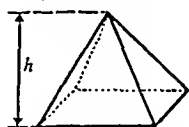


$$A = 6a^2 \quad (260)$$

$$d = a\sqrt{3} = 1.732051a \quad (261)$$

$$V = a^3 \quad (262)$$

2. Pyramid (any base)

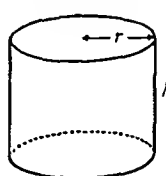


Volume

$$V = \frac{h}{3} A_b \quad (263)$$

(A_b = area of base)

3. Right circular cylinder



Area of convex surface

$$A_c = 2\pi rh = 6.2831853rh \quad (264)$$

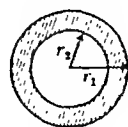
Total surface area

$$\left. \begin{aligned} A &= 2\pi r(r + h) \\ &= 6.2831853r(r + h) \end{aligned} \right\} \quad (265)$$

Volume

$$V = \pi r^2 h = 3.14159265r^2 h \quad (266)$$

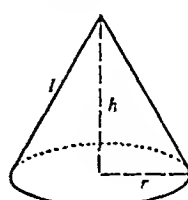
Hollow cylinder



Internal volume

$$\left. \begin{aligned} V_i &= \pi(r_1^2 - r_2^2)h \quad [r_1 \geq r_2] \\ &= 3.14159265(r_1^2 - r_2^2)h \end{aligned} \right\} \quad (267)$$

4. Right circular cone



Area of convex surface

$$\left. \begin{aligned} A_c &= \pi rl = 3.14159265rl \\ &\quad (l = \text{slant height} = \sqrt{r^2 + h^2}) \end{aligned} \right\} \quad (268)$$

Total surface area

$$\left. \begin{aligned} A &= \pi r(r + l) \\ &= 3.14159265r(r + l) \end{aligned} \right\} \quad (269)$$

Volume

$$V = \frac{1}{3} \pi r^2 h = 1.04719755r^2 h \quad (270)$$

ted cone (right circular, plane surfaces parallel)



Area of convex surface

$$A_C = \pi l(r_1 + r_2) = 3.14159265 l(r_1 + r_2) \quad (271)$$

Total surface area

$$A = \pi [r_1(r_1 + l) + r_2(r_2 + l)] \quad (272)$$

Volume

$$V = \frac{\pi h}{3} (r_1^2 + r_1 r_2 + r_2^2) = 1.04719755 h (r_1^2 + r_1 r_2 + r_2^2) \quad (273)$$

arc



Surface area

$$A = 4\pi r^2 = \pi a^2 = 12.5663706 r^2 = 3.14159265 a^2 \quad (274)$$

Volume

$$V = \frac{4\pi r^3}{3} = \frac{\pi a^3}{6} = 4.18879020 r^3 = 0.52359878 a^3 \quad (275)$$

nt of a sphere (cut by a single plane)



Area of convex surface

$$A_C = \pi (r_1^2 + h^2) = 2\pi r_1 h \quad (276)$$

Total surface area

$$A = \pi (2r_1^2 + h^2) \quad (277)$$

Volume

$$V = \frac{\pi h}{6} (3r_1^2 + h^2) = \frac{\pi h^3}{3} (3r_1 - h) \quad (278)$$

$$(\pi = 3.14159265, \pi/6 = 0.52359878, \pi/3 = 1.04719755)$$

nt of a sphere (between two parallel planes)



Area of convex surface

$$A_C = 2\pi r_1 h = 6.2831853 r_1 h \quad (279)$$

Total surface area

$$A = \pi (r_1^2 + 2r_1 h + r_1^2) \quad (280)$$

Volume

$$V = \frac{\pi h}{6} (3r_1^2 + 3r_1 h + h^2) = 0.52359878 h (3r_1^2 + 3r_1 h + h^2) \quad (281)$$

segment of a sphere

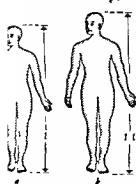


Volume

$$V = \frac{\pi r_1^3 \theta}{270} = 0.011635528 r_1^3 \theta \quad (282)$$

[for θ (= angle between the two planes passing through the centre of the sphere) see (246) and (247)]

odies of the same shape



Bodies of the same shape, i.e., those in which all corresponding linear measurements bear the same ratio $a:b$, have surface areas in the ratio $a^2:b^2$ and weights and volumes in the ratio $a^3:b^3$ (283)

All linear dimensions of body b are 10% greater than those of body a , b has 21% more surface area and 33% more weight

one that this is usually not true of human bodies of different heights

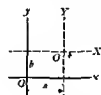
XVI. Formulae of analytical geometry

1. Transformation of rectangular coordinates

The new coordinates are indicated by C , the transformed variables by X, Y , the old coordinates and variables by x, y . For the sake of simplicity the transformation is illustrated in the first quadrant (see section XI, page 138) but the equations are valid for all quadrants.

(a) Translation of coordinate axes

The origin is translated from O to O' , i.e., a distance a in the direction x and a distance b in the direction y



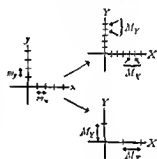
Transformation $\epsilon \rightarrow C$

$$\begin{aligned} X &= x - a \\ Y &= y - b \end{aligned} \quad (284)$$

Transformation $C \rightarrow \epsilon$

$$\begin{aligned} x &= a + X \\ y &= b + Y \end{aligned} \quad (285)$$

(b) Alteration of linear scale



Transformation $\epsilon \rightarrow C$

$$\begin{aligned} X &= \frac{M_x}{m_x} x \\ Y &= \frac{M_y}{m_y} y \end{aligned} \quad (286)$$

Transformation $C \rightarrow \epsilon$

$$\begin{aligned} x &= \frac{m_x}{M_x} X \\ y &= \frac{m_y}{M_y} Y \end{aligned} \quad (287)$$

(c) Translation of axes and alteration of linear scale

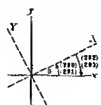
Transformation $\epsilon \rightarrow C$

$$\begin{aligned} X &= \frac{M_x}{m_x} (x - a) \\ Y &= \frac{M_y}{m_y} (y - b) \end{aligned} \quad (288)$$

Transformation $C \rightarrow \epsilon$

$$\begin{aligned} x &= a + \frac{m_x}{M_x} X \\ y &= b + \frac{m_y}{M_y} Y \end{aligned} \quad (289)$$

(d) Rotation of coordinate axes



Transformation $\epsilon \rightarrow C$

$$\begin{aligned} X &= x \cos \beta + y \sin \beta \\ Y &= y \cos \beta - x \sin \beta \end{aligned} \quad (290)$$

or

$$\begin{aligned} X &= \frac{1}{\sqrt{1 + \tan^2 \beta}} (x + y \tan \beta) \\ Y &= \frac{1}{\sqrt{1 + \tan^2 \beta}} (y - x \tan \beta) \end{aligned} \quad (291)$$

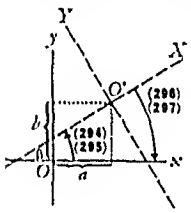
Transformation $C \rightarrow \epsilon$

$$\begin{aligned} x &= X \cos \beta - Y \sin \beta \\ y &= X \sin \beta + Y \cos \beta \end{aligned} \quad (292)$$

or

$$\begin{aligned} x &= \frac{1}{\sqrt{1 + \tan^2 \beta}} (Y - X \tan \beta) \\ y &= \frac{1}{\sqrt{1 + \tan^2 \beta}} (Y + X \tan \beta) \end{aligned} \quad (293)$$

(c) Rotation and translation of the coordinate axes

Transformation $\epsilon \rightarrow C$

$$\left. \begin{aligned} X &= (x-a) \cos \beta + (y-b) \sin \beta \\ Y &= (y-b) \cos \beta - (x-a) \sin \beta \end{aligned} \right\} \quad (294)$$

or

$$\left. \begin{aligned} X &= \frac{x-a + (y-b) \tan \beta}{\sqrt{1 + \tan^2 \beta}} \\ Y &= \frac{y-b - (x-a) \tan \beta}{\sqrt{1 + \tan^2 \beta}} \end{aligned} \right\} \quad (295)$$

Transformation $C \rightarrow \epsilon$

$$\left. \begin{aligned} x &= a + X \cos \beta - Y \sin \beta \\ y &= b + Y \cos \beta + X \sin \beta \end{aligned} \right\} \quad (296)$$

or

$$\left. \begin{aligned} x &= a + \frac{X - Y \tan \beta}{\sqrt{1 + \tan^2 \beta}} \\ y &= b + \frac{Y + X \tan \beta}{\sqrt{1 + \tan^2 \beta}} \end{aligned} \right\} \quad (297)$$

2. Straight line

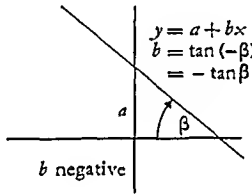
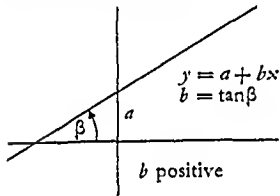
General equation

$$Ax + By + C = 0$$

Equation of slope

$$y = a + bx \quad \text{or} \quad x = \frac{y-a}{b} \quad (299)$$

a = intercept with y axis, b = tangent of the angle of slope β .
Note that $b = \tan \beta$ is valid only when the same unit is used for both coordinate axes.



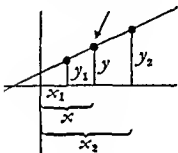
Special cases

$x = a$ is the equation of a line parallel to the y axis (300)

$y = c$ is the equation of a line parallel to the x axis (301)

A straight line is at right angles to another straight line with slope b when its slope is $-1/b$. (302)

Straight line through two points with coordinates $x_1, y_1; x_2, y_2$



$$y = y_1 + \frac{y_2 - y_1}{x_2 - x_1} (x - x_1) \quad (303)$$

This formula is used for linear interpolation.

Example: Tabulated values

x	y
110	83.83
120	95.66

Required: the y value for $x = 116$

$$\text{Solution: } y = 83.83 + \frac{95.66 - 83.83}{120 - 110} (116 - 110) = 90.93$$

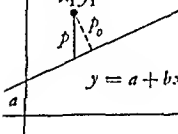
Straight line with slope b through a point x_1, y_1

$$y = y_1 + b(x - x_1) \quad (304)$$

Straight line through the origin and a point x_1, y_1

$$y = \frac{y_1}{x_1} x \quad (305)$$

Length p of the straight line parallel to the y axis between a point x_1, y_1 and the straight line $y = a + bx$

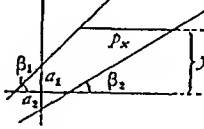


$$p = y_1 - a - bx_1 \quad (306)$$

Shortest (orthogonal) distance p_0 between a point and the straight line $y = a + bx$

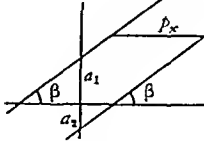
$$p_0 = \frac{y_1 - a - bx_1}{\sqrt{1 + b^2}} \quad (307)$$

Distance p_x parallel to the x axis at a height y_p between two straight lines $y = a_1 + b_1x$ and $y = a_2 + b_2x$



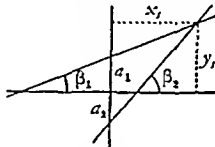
$$p_x = \left| \frac{y_p - a_1}{b_1} - \frac{y_p - a_2}{b_2} \right| \quad (308)$$

Distance p_x parallel to the x axis between two parallel lines $y = a_1 + bx$ and $y = a_2 + bx$ [special case of (308) with $b_1 = b_2$]



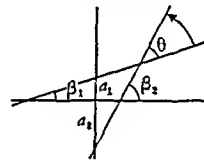
$$p_x = \left| \frac{a_1 - a_2}{b} \right| \quad (309)$$

Coordinates of the intersection of two straight lines $y = a_1 + b_1x$ and $y = a_2 + b_2x$



$$\left. \begin{aligned} x_s &= \frac{a_2 - a_1}{b_1 - b_2} \\ y_s &= \frac{b_1 a_2 - b_2 a_1}{b_1 - b_2} \end{aligned} \right\} \quad (310)$$

Angle θ between two straight lines with slopes b_1 and b_2



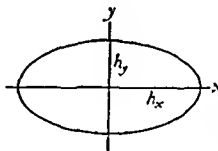
$$\tan \theta = \frac{b_2 - b_1}{1 + b_1 b_2} \quad (311)$$

The angle θ is the positive angle through which the first straight line must be rotated in order that it shall coincide with the second straight line. Note that equation (311) is valid only when the same unit is used for both coordinate axes.

3. Ellipse

Standard equation in rectangular coordinates (the principal axes):

$$\frac{x^2}{a^2} + \frac{y^2}{b^2} = c^2 \quad (312)$$

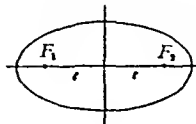


a and b determine the relation between the two semi-axes and thus the shape of the ellipse.

If h_x is the semi-major, h_y the semi-minor axis, equation (312) becomes

$$\frac{x^2}{h_x^2} + \frac{y^2}{h_y^2} = 1 \quad \left\{ \begin{aligned} h_x^2 &= c^2 a^2 \\ h_y^2 &= c^2 b^2 \end{aligned} \right. \quad (313)$$

The focal width $F_1 F_2$ is given by

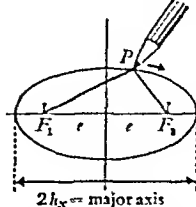


$$2e = 2\sqrt{h_x^2 - h_y^2} \quad (314)$$

e is known as the linear eccentricity.

If s is the sum of the distances from a point P on the curve to the foci F_1 and F_2 , then

$$s = 2h_x = \text{major axis} \quad (315)$$



Any desired ellipse may therefore be drawn by means of a thread of length $2h_x$ attached to the foci, e being determined from equation (314).

For area and circumference of the ellipse see equations (255) and (256) on page 142.

ts (pages 146-196)	
rd	146
ductory definitions	146
lation and sample	146
able and event	147
quency, probability, compound events	147
crete probability distribution	148
tinuous probability distribution	151
mates	153
expectation and bias	153
consistency	153
fficiency	153
fficient estimates	154
idence limits and tolerance limits	154
Confidence limits for continuous and discrete distributions	154
Tolerance limits for continuous distributions	155
Distribution-free confidence and tolerance limits	155
istical significance tests	156
ntroduction	156
Significance limits	156
Significance tests	157
ameters	159
Mean and variance of the population	159
Transformations	159
.....	159
.....	160
.....	160
continuous distributions	161
Relations between mode, median and mean	161
The sign test	161
ic normal distribution	161
Definition and characteristics	161
The standardized normal distribution	162
Tables of the standardized normal distribution	162
Conversion of a normal distribution into the standardized form and vice versa	162
The probit transformation	163
Fitting of normal curves to samples	163
.....	165
.....	165
.....	166
The central limit theorem	166
distributions closely allied to the normal distribution	166
The Student distribution	166
The χ^2 distribution	166
The F -distribution (variance-ratio distribution)	168
he normally distributed population: Confidence and tolerance intervals	169
Confidence intervals for the mean μ	169
Tolerance intervals	169
Confidence intervals for the standard deviation σ	169
he normally distributed population: Extreme range and extreme deviations	170
The extreme range	170
Testing extreme ranges and extreme deviations	170
he normally distributed population. Comparison of a sample with the hypothetical population	171
Comparison of the sample and population standard deviations s and σ (or of the variances s^2 and σ^2)	171
Comparison of the sample and population means \bar{x} and μ	171
16. The normally distributed population: Comparison of two samples	172
A Comparison of variances	172
B Comparison of means when $\sigma_1^2 = \sigma_2^2$	172
C Comparison of means when $\sigma_1^2 \neq \sigma_2^2$	173
D Testing pair differences	173
E Tests for two samples using the extreme range	173
17. The normally distributed population: Testing several samples	173
A Testing variances	173
B Testing means: simple analysis of variance	173
.....	174
.....	174
.....	176
.....	177
.....	177
.....	177
.....	178
19 The bivariate normal distribution: Regressions of the second kind	179
A The correlation coefficient	179
B SPEARMAN'S coefficient of rank correlation	181
C Significance tests	181
D Confidence and tolerance limits	182
20. The binomial distribution	183
A General	183
B Parameters	184
C Cumulative probabilities	184
D The binomial and the normal distribution	185
E The binomial and the Poisson distribution	186
F Confidence limits and significance limits	186
G Miscellaneous	187
21. The Poisson distribution	187
A General	187
B The addition theorem for the Poisson distribution	188
C Parameters and their estimates	188
D Transformations	188
E Confidence limits and significance limits	189
22. The hypergeometric distribution	189
A General	189
B Parameters	191
C The hypergeometric distribution and other distributions	191
D Significance limits (fourfold table test)	191
23. Testing frequencies	191
A Samples from binomially distributed populations	191
B Samples from multinomially distributed populations	192
C Samples from Poisson distributions	192
24 Rank tests	192
A Ranking	192
B The WILCOXON test for two samples	192
C The WILCOXON test for pair differences	192
D HALDANE'S test for chance order in series	193
E The maximum test for pair differences	193
25	193
.....	193
.....	193
.....	194
.....	194
.....	195
.....	195
.....	195
26 Sequential analysis	196
References	196

(For references see page 196; for index see pages 197 and 198)

In the limited space here available it is impossible to give more than a brief explanation of the statistical tables on pages 10-131. The following description is therefore limited to those fundamentals the non-mathematician requires to enable him to solve simple statistical problems.

The calculation of probabilities by statistical methods is an essential step in the proper interpretation of experimental results that comply with certain basic laws but are at the same time subject to modification by unknown factors, in other words, to so-called 'chance' variation. This holds not only for the empirical sciences, the exact as well as the biological, but in a wider sense also for the abstract sciences:

On peut même dire à parler en rigueur, que presque toutes nos connaissances ne sont que probables; et dans le petit nombre des choses que nous pouvons savoir avec certitude, dans les sciences mathématiques elles-mêmes, les principaux moyens de parvenir à la vérité, l'induction et l'analogie, se fondent sur les probabilités... (LAPLACE, 1820)¹.

One reason for the physician's frequent mistrust of statistical methods is epitomized in the well-known allegation that 'you can prove anything with statistics'. Some prejudice against mathematics is also understandable in a profession in which intuitive reasoning is generally preferred. These are sentiments without any logical basis. Statistics is one of the most vigorous branches of mathematics, and its techniques for the disciplined assessment of observational data can be readily mastered. Furthermore, it should not be forgotten that every medical diagnosis represents the result of an intentional or unintentional calculation of probabilities.

This critical attitude towards statistics has its origin in their improper use as well as in their false interpretation. The statistical method is no more than another scientific method and cannot by its nature provide proof or disproof. On the other hand it constitutes the only method of subjecting values liable to chance variation (stochastic variables) to fixed and reproducible criteria based on logical mathematical considerations. The converse of the saying quoted is therefore much nearer the truth, namely that *no scientific investigation is capable of proving anything without the aid of statistics*. Human judgement is influenced to a very large extent by the subconscious wish and by the deep-rooted tendency – even in the worst of pessimists – to overrate one's own chances. The most careful investigator can be led astray by these psychological factors if he fails to arm himself against them with an adequate measure of self-control:

Le sentiment par lequel l'homme s'est placé longtemps au centre de l'univers en se considérant comme l'objet spécial des soins de la nature, porte chaque individu à se faire le centre d'une sphère plus ou moins étendue, et à croire que le hasard a pour lui des préférences. Soutenus par cette opinion, les joueurs exposent souvent des sommes considérables à des jeux dont ils savent que les chances leur sont contraires. Dans la conduite de la vie, une semblable opinion peut quelquefois avoir des avantages; mais le plus souvent elle conduit à des entreprises fâcheuses. Ici, comme en tout, les illusions sont dangereuses et la vérité seule est généralement utile.

Un des grands avantages du Calcul des Probabilités est d'apprendre à se défier des premiers aperçus. Comme on reconnaît qu'ils trompent souvent lorsqu'on peut les soumettre au calcul, on doit en conclure que sur d'autres objets il ne faut s'y livrer qu'avec une circonspection extrême (LAPLACE, 1820)¹.

'The wish' as 'father to the thought' may be an indispensable stimulus to research, but it has also been responsible – in the guise of 'our experience' or 'our opinion' backed by a few percentages – for much misunderstanding. One need only reflect on the wealth of new treatments and new drugs which after an enthusiastic reception have been allowed to fall quietly into oblivion.

Many a research worker in the past could have spared himself much wasted time and effort had he submitted his observations and hypotheses to statistical test before publication. Recognition of this fact has clearly become general during the last decades, and close links have now been established between clinical medicine and statistics.

The growing use of statistical methods, however, is not without its own dangers. The general tendency is to overrate any new research tool, particularly when it is unfamiliar and complicated in operation. Too much uncritical dependence is placed on the results obtained; the limitations of the method may not be clearly recognized and the experimental data may be inadequately checked. Statistical methods obviously allow of no such dispensation. On the other hand, the beginner will find that with increasing experience statistical ways of thinking will not only render him more circumspect but give him a deeper insight.

1. Introductory definitions*

An experiment subject to chance factors may be compared to an operation such as the drawing of numbers in a lottery. Imagine a box containing balls bearing the numbers 0, 1, 2, ..., 9. These are thoroughly mixed before the draw is commenced. The player drawing the balls is supposed to have no influence on the selection.

Using this analogy, we designate

– the mixing of the balls as the *randomization* of the experimental material; (316)

– the numbers 0, 1, 2, ..., 9 distinguishing the balls as *variables* or *attributes*; (317)

– the aggregate number of balls in the box as the *parent population*; (318)

– a draw as a *trial*; (319)

– N trials as *random sampling*; (320)

– the result of the trial represented by the drawing of the number 5 as the *random event* 5; (321)

– the result of N trials as a *random sample* of size N , or briefly as a *sample* N ; (322)

– the succession of events as a *random sequence* (in the numbered balls analogy it is the random series of numbers, or *random numbers*); (323)

– the relative frequency of the variate values in the population as the *probabilities* with which these values will be drawn; (324)

– the relative frequency of the variate values in the sample as *estimate* of their probability; (325)

– the distribution of the probabilities of the different variate values as *probability distribution*, or briefly as *distribution*. (326)

Some of these definitions will be discussed in more detail later in this chapter.

2. Population and sample

A population is finite or infinite when the trials (draws) can be repeated a finite or infinite number of times. (327)

A finite population, such as a finite number of balls in a box, can be converted into an effectively infinite one by putting the balls back into the box after each draw. Such an operation is known as *sampling with replacement*. (328)

From an infinite population an infinite number of samples can be taken, for example all of the same size N . The totality of such samples of size N is known as the *sampling population* N and their probability distribution as the *sampling distribution* N . (329)

An infinite sampling population can also be taken from a finite population in a manner similar to that in (328), i.e., by returning the whole of the first sample to the box, drawing a second sample of the same size, returning this sample also to the box, and so on. *All sampling populations can therefore be regarded as infinite*. This is one of the fundamental concepts of mathematical statistics. (330)

Quantities such as mean value and variance which relate to the population are known as *parameters*, their counterparts in the sample as *statistics*. (331)

Symbols relating to the population are here printed in bold type whenever it is necessary to distinguish them from symbols relating to samples. Exceptions are the symbols for mean value and variance: these are respectively μ and σ^2 for the population and \bar{x} and s^2 for the sample. (332)

* The mathematician will appreciate that this presentation is more readily understandable by non-mathematicians than a strictly mathematical one.

table and event

... (333)

is an event, then the non-occurrence of A is its *complementary event*, designated here as non- A . Examples: success or failure, alive or dead, 6 or non-6 in die rolling, etc. (334)

complementary event non- A is often an event B . For example, a girl can be born instead of a boy. Such events known as *mutually exclusive events*, denoted by A or B , A, B and non- A in (334) are therefore by definition mutually exclusive events (335)

... (336)

... (337)

the occurrence (or non-occurrence) of an event A is noted by the condition that an event B has occurred occurs simultaneously, cf. (336), then event A is said to be a *conditional event*, denoted by $A|B$ and read as 'if A under the condition B '. B can represent several situations (338)

stochastic variables can be denoted by numbers, for example 1 for success, 0 for failure (339)

events are already numbers they are here denoted by symbols that other symbols are not in general use, as in case of some sampling distributions (340)

(within a finite interval) takes only a finite number of values it is known as a *discrete random variable* or *discrete*. In this case x changes by discrete amounts. Examples: 0, 1, 2, 3, successes, 25, 26, 27, respirations, (341)

the numbers 1, 2, 3, ... denote the smallest, second smallest, third smallest value, etc., the series is known as a *discrete series*. Examples: heights of men, their exact heights being known (342)

x can take all possible values in some interval it is known as a *continuous random variable* or *variable*. In this case x changes continuously. Examples of continuous variables are length, area, volume, weight, temperature, time and contraction, i.e., variables that can be *measured* (343)

in practice, continuous variables do not exist since all measured values are rounded values. For example, when the smallest interval a balance can measure is a milligramme, the weight measured will be rounded off to the nearest (344)

in the case of discrete variables the same value may occur (345)

two or more identical values occur in a sample of a 'censored' variable they are known as *tied* or *tied values* (346)

4. Frequency, probability, compound events

... (34)

to mean the relative frequency
The relative frequency multiplied by 100 is known as the *percentage frequency*. Example 2. In 81 operations there are 3 fatalities. The percentage frequency is then $(3/81) \times 100 = 3.7\%$. (34)

The following symbols are used here for probability
'Probability' in general, ... Prob
Probabilities of mutually exclusive events, ... P
Probabilities of two complementary events, ... p and q (345)

In a later section the symbols α and P^* will also be used [cf. (371) and (379)] (346)

In (324) probability was defined as the *relative frequency of a variable* [or of an event, cf. (333)] in the population. Propositions (350)-(352) follow directly from this definition (347)

Every probability is a number between zero and one
 $0 \leq \text{Prob} \leq 1$ (350)

An impossible event has a probability of zero, a certain event a probability of one (351)

The converse of (351) is not valid
An event with a probability of zero is an *almost impossible* event, an event with a probability of one an *almost certain* event. (352)

The sum of the probabilities of all mutually exclusive events E_1, E_2, \dots, E_N in a single population is equal to one
 $\text{Prob}(E_1 \text{ or } E_2 \text{ or } \dots \text{ or } E_N)$
 $= P_1 + P_2 + \dots + P_N = 1$
where the total of all mutually exclusive events is $N + 1$, and (cf. (335)) (353)

$\text{Prob}(E \text{ or non-}E) = p + q = 1$
It follows from (353) that a population with many mutually exclusive events can be converted in various ways into one with two complementary events (354)

For example
 $\text{Prob}[(E_1 \text{ or } E_2) \text{ or } (E_3 \text{ or } \dots \text{ or } E_N)]$
 $= \text{Prob}(E) + \text{Prob}(\text{non-}E)$
 $= P + Q$
where the total number of mutually exclusive events is $N + 1$ (348)

From (353) it follows that
Of the mutually exclusive events A, B, \dots , the probability that either the event A or the event B will occur is equal to the sum of their probabilities, provided that the events are from one and the same population
 $\text{Prob}(A \text{ or } B \text{ or } \dots) = P_A + P_B + \dots$ (355)

Example 6 [of (355)] *Incorrect application* Assuming that the mortality of 85-year-olds is 0.5 and that of 86-year-olds 0.6, then

the statement that there is a 1.1 probability of an 85-year-old dying either at 85 or at 86 is false. Here the error is already indicated by the probability figure of 1.1, which according to (350) is an impossibility, but it might well have been overlooked had the figure been 0.4, as in example 5. The error arises from the fact that mutually exclusive events from *different* populations, that of the 85-year-olds and that of the 86-year-olds, have been added together.

The probability of two simultaneous or successive events A and B is equal to the probability of the event A multiplied by the probability of the event B under the condition A , or to the probability of the event B multiplied by the probability of the event A under the condition B . On conditioned events see (338).

$$\text{Prob}(A \text{ and } B) = \text{Prob}(A) \times \text{Prob}(B | A) \\ = \text{Prob}(B) \times \text{Prob}(A | B) \quad (356)$$

Example 7 [of (356)]. A box contains N balls, x red and $N - x$ white. A sample consisting of two balls is drawn *without replacement*. What is the probability of drawing (a) two red balls, (b) a red and then a white ball, (c) a red and a white ball in any order?

(a) The probability of a red ball at the first draw is x/N . The conditioned probability of a red ball at the second draw (when there is one red ball less in the box) is $(x-1)/(N-1)$. The probability of drawing two red balls is therefore

$$\text{Prob}(\text{red, red}) = \frac{x}{N} \times \frac{x-1}{N-1}$$

$$(b) \text{ Prob}(\text{red, white}) = \frac{x}{N} \times \frac{N-x}{N-1} \\ = \frac{N-x}{N} \times \frac{x}{N-1} = \text{Prob}(\text{white, red})$$

$$(c) \text{ Prob}(\text{red and white}) \text{ or } \text{Prob}(\text{white and red}) \\ = \text{Prob}(\text{red, white}) + \text{Prob}(\text{white, red}) \\ = 2x(N-x)/N(N-1)$$

Example 8 [of (356)]. From the same box as in example 7 a sample of the same size is taken, but *with replacement*. In this case the probabilities are as follows:

(a) The probability of a red ball at the first draw remains x/N . Since this ball is replaced in the box, the probability of a red ball at the second draw is the same:

$$\text{Prob}(\text{red, red}) = \frac{x}{N} \times \frac{x}{N}$$

$$(b) \text{ Prob}(\text{red, white}) = \frac{x}{N} \times \frac{N-x}{N} \\ = \frac{N-x}{N} \times \frac{x}{N} = \text{Prob}(\text{white, red})$$

$$(c) \text{ Prob}(\text{red and white}) \text{ or } \text{Prob}(\text{white and red}) \\ = \text{Prob}(\text{red, white}) + \text{Prob}(\text{white, red}) \\ = 2x(N-x)/N^2$$

From example 7 it will be seen that the probabilities change with each draw, i.e., each successive draw is *dependent* on the previous one. The corresponding statistical expressions are *dependent trials* and *dependent events*. In example 8 the second draw is unaffected by the previous one, in which case the trials and events are *independent*.

In other words, in the collection of samples from *finite* populations (no replacement), the trials and events are *dependent* on one another; in the collection of samples from *infinite* populations (replacement), they are *independent* of one another.

Two simultaneous or successive events are known as stochastically *dependent* events when in (356) the conditioned and the absolute probability of an event are *not* the same, i.e., when

$$\text{Prob}(A|B) \neq \text{Prob}(A), \text{ or } \text{Prob}(B|A) \neq \text{Prob}(B).$$

Two simultaneous or successive events are known as stochastically *independent* events when in (356) the conditioned and the absolute probability of an event are *the same*, i.e., when

$$\text{Prob}(A|B) = \text{Prob}(A), \text{ or } \text{Prob}(B|A) = \text{Prob}(B).$$

From (356) and (359) it follows that the two events A and B are stochastically independent of one another when the probability of their simultaneous or successive occurrence is equal to the product of their probabilities:

$$\text{If } \text{Prob}(A \text{ and } B) = \text{Prob}(A) \times \text{Prob}(B) \\ \text{then } A \text{ and } B \text{ are stochastically independent of one another.} \quad (360)$$

In (358)–(360) the expressions ‘dependent’ and ‘independent’ are coupled with the qualification ‘stochastic’. This is a precautionary measure of the statistician. In (358)–(360) a *factual conclusion is reached on the basis of a mathematical result*. If such conclusions lie wholly within the domain of the probability calculation the expressions ‘dependent’ and ‘independent’ are completely valid, as in examples 7 and 8 under (356). However, if they are extended beyond the mathematical domain into those of physics, chemistry, physiology, etc., then the qualification ‘stochastic’ is necessary since the conceptions ‘dependent’ and ‘independent’ do not necessarily imply a *causal* connection. Stochastically independent events can very well be dependent on one another in reality. The conclusion ‘independent’ implies only *actual independence of the events*. It can be accepted if it is not incompatible with the physical circumstances. On the other hand it can be regarded as *proof* if independence were *presumable* from the physical circumstances and the mathematical treatment led to the same result. For this reason the converse of (360) should also be noted:

If A and B are events independent of one another, then the probability of their simultaneous or successive occurrence is equal to the product of their probabilities:

$$\text{Prob}(A \text{ and } B) = \text{Prob}(A) \times \text{Prob}(B) \\ (\text{when } A \text{ and } B \text{ are independent of one another}).$$

Example 9 [of (362)]. A box contains the events ‘+’ and ‘-’ equal numbers, so that the probabilities are $1/2$. Samples are lected with replacement, so that in accordance with (357) the events are independent of one another. What is the probability of drawing ‘+’ 5, 6 or 7 times in succession? The respective probabilities $(1/2)^5$, $(1/2)^6$, $(1/2)^7$, or 0.03125, 0.015625, 0.0078125.

Example 10 [of (362)]. An infinite population contains the events A and B with the probabilities p and q respectively. What are the probabilities of the events AA , AB , BA , BB in two draws?

Event	Probability
AA	$p \times p = p^2$
AB	$p \times q$
BA	$q \times p$
BB	$q \times q = q^2$

$$\left. \begin{array}{l} p \times q \\ q \times p \end{array} \right\} = 2pq = p^2 + 2pq + q^2 = (p + q)^2 = 1^2 = 1, \text{ as it should be according to (353)}$$

In the expression $p^2 + 2pq + q^2$ the individual terms represent the *probability distribution* for the events two As , one A , no As (provided that no importance is attached to the order in event one A). A *sampling distribution* [cf. (329)] is thus obtained samples of size 2 from an infinite population, the complemen variables A or B , and the probabilities p and q . From this example it will be seen intuitively how samples with 3, 4, ... draws can be dealt with: the sampling distributions can be written in accordance with (113) as developments of $(p + q)^3$, $(p + q)^4$, ... Cf. Binomial distribution, page 183.

5. Discrete probability distribution

Example 10 under (362) demonstrated a simple sampling distribution of practical importance that will be further discussed later in this chapter. At this point, discussion will be limited to a few conceptions related to such a distribution.

Given an infinite population with the events $x = 0, 1, 2, \dots$, and the probabilities P_x , then:

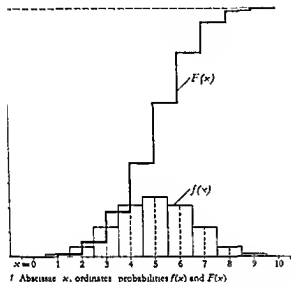
x	$P_x = f(x)$	$\sum_{k=0}^{x-1} P_k = F(x)$
0	0.0010	0.0010 = P_0
1	0.0098	0.0108 = $P_0 + P_1$
2	0.0439	0.0547 = $P_0 + P_1 + P_2$
3	0.1172	0.1719 = $P_0 + P_1 + P_2 + P_3$
4	0.2051	0.3770 etc.
5	0.2460	0.6230
6	0.2051	0.8281
7	0.1172	0.9453
8	0.0439	0.9892
9	0.0098	0.9990
10	0.0010	1.0000

a column $P_x = f(x)$ gives the probabilities for the events $x = 0, x = 1, x = 2$, etc :

rding to (324) this is the probability distribution for the $x = 0, x = 1, x = 2$, etc, denoted by $f(x)$. } (343)

$$P_x = \begin{matrix} x=0 & x=1 & x=2 & \dots & x=N \end{matrix} \quad (344)$$

these data may be represented graphically:



Since x is a discrete variable [cf. (341)] the distributions $f(x)$ and $F(x)$ give stepped curves. It follows that

discrete random variable has a discrete probability distribution } (345)

ie probabilities are dependent on x , i.e., for every value of x there is a definite probability $f(x)$ and $F(x)$ are functions of x whence the use of the symbols f and F (the Greek letters φ and Φ are also frequently used) The pattern of probabilities can be expressed by a mathematical formula in some other appropriate manner } (346)

In figure 1 the probabilities $f(x)$ and $F(x)$ are shown as stepped curves in order to emphasize the similarity between discrete and continuous distributions (cf. Fig. 8). In fact, such a stepped curve could represent a "granulated" distribution [cf. (344)] in which the values of x have been rounded off to whole numbers. In this case 4 events between 4.5 and 5.5, for example, would be assigned to event 5. For this reason, another method is preferred here for presenting discrete distributions which shows clearly that the events x are discrete

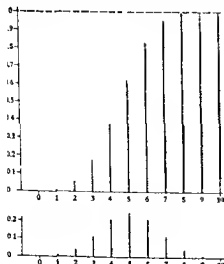


Fig. 2

In the cumulative distribution $F(x)$ representing the probabilities of the events $x = 0, x = 0$ or 1, $x = 0$ or 1 or 2, etc, the expression $x = 0, 1$ will in future be used in place of $x = 0$ or 1. Prob ($x = 0, 1$) can also be written as Prob ($x \leq 1$). From (344) another notation is Prob ($x < 2, 3, \dots, N$), equivalent to Prob ($x < 2$)

In general, the following expressions are valid for such discrete distributions.

$$\begin{aligned} \text{Prob}(x < k+1) &= \text{Prob}(x \leq k), \text{ or} \\ \text{Prob}(x < k) &= \text{Prob}(x \leq k-1) \\ \text{and Prob}(x > k-1) &= \text{Prob}(x \geq k), \text{ or} \\ \text{Prob}(x > k) &= \text{Prob}(x \geq k+1) \end{aligned} \quad (347)$$

With increasing values of k , the distribution $F(x)$ thus produces continuously the probabilities for $x \leq k$ or $x < k+1$. } (348)

Conversely, with decreasing values of k the cumulative distribution $\sum_{x=k}^N P_x$ from N in the direction of zero produces continuously the probabilities for $x \geq k$ or $x > k-1$ } (349)

For discrete distributions in general the following should be noted:

$$\begin{aligned} \text{Prob}(x = k) &= P_x = f(k) \end{aligned} \quad (370)$$

$$\text{Prob}(x \neq k) = 1 - P_x = 1 - f(k) \quad (371)$$

$$\begin{aligned} \text{Prob}(x \leq k) &= \text{Prob}(x < k+1) \\ &= \sum_{x=0}^k P_x, \text{ best formula if } k \leq N/2 \end{aligned} \quad (372)$$

$$= 1 - \sum_{x=k+1}^N P_x, \text{ best formula if } k \geq N/2 \quad (a)$$

$$= F(k), \text{ best formula if } F(x) \text{ is given} \quad (b)$$

$$= 1 - \sum_{x=k+1}^N P_x, \text{ best formula if } \sum_{x=0}^N P_x \text{ is given} \quad (c)$$

$$\begin{aligned} \text{Prob}(x \geq k) &= \text{Prob}(x > k-1) \\ &= 1 - \sum_{x=0}^{k-1} P_x, \text{ best formula if } k \leq N/2 \end{aligned} \quad (373)$$

$$= \sum_{x=k}^N P_x, \text{ best formula if } k \geq N/2 \quad (a)$$

$$= 1 - F(k-1), \text{ best formula if } F(x) \text{ is given} \quad (b)$$

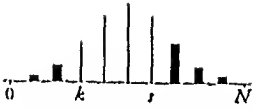
$$= \sum_{x=k}^N P_x, \text{ best formula if } \sum_{x=0}^N P_x \text{ is given} \quad (c)$$

$$\begin{aligned} \text{Prob}(k \leq x \leq i) &= \text{Prob}(x = k, k+1, \dots, i) \\ &= \sum_{x=k}^i P_x, \text{ best formula if } i - k \leq N/2 \end{aligned} \quad (374)$$

$$= 1 - \sum_{x=0}^{k-1} P_x - \sum_{x=i+1}^N P_x, \text{ best formula if } i - k \geq N/2 \quad (a)$$

$$= F(i) - F(k-1), \text{ best formula if } F(x) \text{ is given} \quad (b)$$

$$= \sum_{x=k}^i P_x - \sum_{x=0}^N P_x, \text{ best formula if } \sum_{x=0}^N P_x \text{ is given} \quad (c)$$



$$\left. \begin{aligned} &\text{Prob}(x \leq k-1) + \text{Prob}(x \geq s+1) \\ &\Rightarrow \text{Prob}(x < k) + \text{Prob}(x > s) \end{aligned} \right\} \quad (375)$$

$$\Rightarrow 1 - \sum_k \dot{P}_x, \text{ best formula if } s - k \leq N/2 \quad (a)$$

$$\Rightarrow \sum_0^{k-1} \dot{P}_x + \sum_{s+1}^N \dot{P}_x, \text{ best formula if } s - k \geq N/2 \quad (b)$$

$$\Rightarrow 1 - F(x) + F(k-1), \text{ best formula if } F(x) \text{ is given} \quad (c)$$

$$\Rightarrow 1 - \sum_k \dot{P}_x + \sum_{s+1}^N \dot{P}_x, \text{ best formula if } \sum_x \dot{P}_x \text{ is given} \quad (d)$$

In (370)–(375) the best formulae for use in each particular case are indicated. As a rule, the user must calculate \dot{P}_x himself and then proceed with the formulae (a) or (b). The editors know of extensive tabulations of $\sum_x \dot{P}_x$ only for the Poisson distribution², of $\sum_x \dot{P}_x$ only for the binomial distribution^{3,4}, of $\sum_x \dot{P}_x | N, n, k$ only for the hypergeometric probability distribution⁵. Some publications^{2,3,5} include also tabulated values of $f(x)$.

Example 11. Using the formulae (a) or (b) in (370)–(375), the probabilities for $k=2$ and $s=8$ are calculated from the values of $f(x)$ given in the table on page 148.

$$(370): \text{Prob}(x=2) = \dot{P}_2 = 0.0439$$

$$(371): \text{Prob}(x \neq 2) = 1 - \dot{P}_2 = 0.9561$$

$$(372): \text{Prob}(x \leq 2) = \dot{P}_0 + \dot{P}_1 + \dot{P}_2 = 0.0547$$

[by formula (a), since $k < N/2$]

$$(373): \text{Prob}(x \geq 2) = 1 - (\dot{P}_0 + \dot{P}_1) = 0.9892$$

[by formula (a), since $k < N/2$]

$$(374): \text{Prob}(2 \leq x \leq 8) = \text{Prob}(x=2, 3, \dots, 8)$$

$$= 1 - (\dot{P}_0 + \dot{P}_1) - (\dot{P}_9 + \dot{P}_{10}) = 0.9784$$

[by formula (b), since $s - k > N/2$]

$$(375): \text{Prob}(x \neq 2, 3, \dots, 8) = (\dot{P}_0 + \dot{P}_1) + (\dot{P}_9 + \dot{P}_{10}) = 0.0216$$

[by formula (b), since $s - k > N/2$]

Example 12. What is the probability of the event 'x at least equal to 1'? This is the same as saying 'x equal to 1 or more' (cf. page 132), and calculation using (373a) gives

$$\text{Prob}(x \geq 1) = 1 - \dot{P}_0 = 0.9990$$

Example 13

Confidence intervals* and significance limits
(Cf. also sections 8 and 9, pages 154–159)

A. One-sided significance limits

Given α , where $0 < \alpha \leq 0.5$, determine x_1 and x_r in such a way that

$$\left. \begin{aligned} &\text{Prob}(x \leq x_1) = P_1 = \sum_0^{x_1} \dot{P}_x \leq \alpha \quad \text{and} \\ &\text{Prob}(x \leq x_1 + 1) = \sum_0^{x_1+1} \dot{P}_x > \alpha \end{aligned} \right\} \quad (376)$$

$$\left. \begin{aligned} &\text{Prob}(x \geq x_r) = P_r = \sum_{x_r}^N \dot{P}_x \leq \alpha \quad \text{and} \\ &\text{Prob}(x \geq x_r - 1) = \sum_{x_r-1}^N \dot{P}_x > \alpha \end{aligned} \right\} \quad (377)$$

For $\alpha = 0.10$, $x_1 = 2$ and $x_r = 8$; for $\alpha = 0.025$, $x_1 = 1$ and $x_r = 9$.

The following definitions follow from the above example:

α is the *postulated or nominal one-sided significance probability* (378)

P is the *actual one-sided significance probability*, P_1 being the *left (lower)* and P_r the *right (upper)* level, with P_1 and $P_r \leq \alpha$ (379)

x_1 is the *left (lower)* and x_r the *right (upper)* significance limit (380)

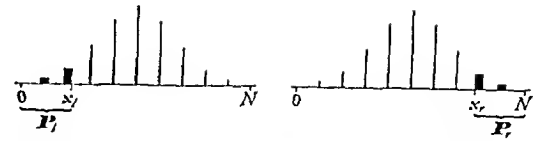


Fig. 3. One-sided significance limits of discrete distributions.

It should be noted that

– if x attains or exceeds (to the left) the *left (lower)* significance limit x_1 , then in a *one-tailed test*

$$\text{Prob}(x \leq x_1) \leq \alpha = \text{Prob}(x < x_{1+1}) \quad (3)$$

– if x attains or exceeds (to the right) the *right (upper)* significance limit x_r , then in a *one-tailed test*

$$\text{Prob}(x \geq x_r) \geq \alpha = \text{Prob}(x > x_{r-1}) \quad (3')$$

– rules (381) and (382) are valid for *all* significance limits of *discrete* distributions tabulated in these *Tables*. Elsewhere, significance limits of discrete distributions may be found which must be exceeded in an *outward* direction if, for example, they are to satisfy the rule $P_1 \leq \alpha$.

– as a rule the *actual* significance probability P in *discrete* distributions is *smaller* than the *nominal* α , for small values of N often considerably smaller. With increasing values of N this difference decreases rapidly. (In example 13 with $\alpha = 0.10$ or 0.025 , the corresponding values of P are 0.0547 or 0.0108 . In this case the actual significance probability amounts to only about 50% of the nominal.) (38)

The following definitions should also be noted:

The range between $x_1 + 1$ and N or between zero and $x_r - 1$ is the *one-sided confidence interval*. (385)

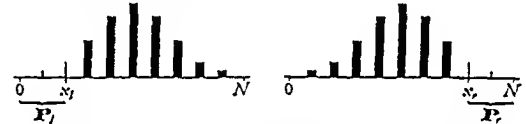


Fig. 4. One-sided confidence intervals for discrete distributions.

x_1 or x_r is the *one-sided confidence limit* when the other limit lies at N or zero. (386)

The probabilities $1 - P_1 \geq 1 - \alpha$ and $1 - P_r \geq 1 - \alpha$ are the *one-sided confidence probabilities*:

$$\text{Prob}(x_1 < x \leq N) = 1 - P_1 = 1 - \sum_0^{x_1} \dot{P}_x \geq 1 - \alpha \quad (387)$$

$$\text{Prob}(0 \leq x < x_r) = 1 - P_r = 1 - \sum_{x_r}^N \dot{P}_x \geq 1 - \alpha \quad (388)$$

From (380) and (386) it will be seen that significance limits and confidence intervals are determined mathematically according to the same principles. (389)

B. Two-sided significance limits

If a left and a right significance limit are determined jointly for a discrete distribution according to rules (376) and (377), then for the two together $P_1 + P_r \leq 2\alpha$. (390)

In this case the following definitions apply:

2α is the *postulated or nominal two-sided significance probability*. (391)

$P_1 + P_r$ is the *actual two-sided significance probability* [note also (384)], where $P_1 = P_r$ in symmetrical distributions and $P_1 \neq P_r$ in unsymmetrical distributions, although both satisfy rules (376) and (377) (cf. Fig. 5). (392)

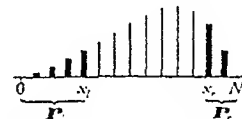


Fig. 5. Two-sided significance limits for discrete (unsymmetrical) distributions.

x_1 and x_r are the *one-sided confidence limits* (with P_1 and $P_r \leq \alpha$) (393)

It should be noted that

when x attains or exceeds (outwards) one of the two significance limits x_1 or x_2 , then in a two-sided test

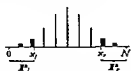
$$\left. \begin{aligned} \text{Prob}(x \leq x_1) + \text{Prob}(x \geq x_2) &\leq 2\alpha = \\ \text{Prob}(x < x_{1.1}) + \text{Prob}(x > x_{2.1}) \end{aligned} \right\} \quad (394)$$


Fig 6 Two-sided significance limits for discrete (symmetrical) distributions

The following definitions should also be noted

The range between $x_1 + 1$ and $x_2 - 1$ is the two-sided confidence interval, or briefly *confidence interval*

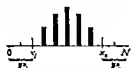
$$\left. \right\} \quad (395)$$


Fig 7 Two-sided confidence interval for discrete distributions

x_1 and x_2 are the two-sided confidence limits, or briefly *confidence limits*, whereby it should again be noted that significance limits and confidence intervals are determined mathematically according to the same principles

$$\left. \right\} \quad (396)$$

The probability $1 - \sum_{x_1}^x f(x) - \sum_{x_2}^x f(x) \approx 1 - 2\alpha$ is the actual two-sided confidence probability, or briefly *confidence probability*

$$\left. \right\} \quad (397)$$

$$\begin{aligned} \text{Prob}(x_1 < x < x_2) &= 1 - \sum_{x_1}^x f(x) - \sum_{x_2}^x f(x) \\ &= 1 - \sum_{x_1}^x f(x) - \sum_{x_2}^x f(x) \approx 1 - 2\alpha \end{aligned}$$

8. Continuous probability distribution

A comparison of Figures 1 and 8 reveals the similarity between discrete and continuous distributions. When the distribution shown

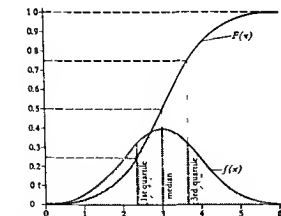
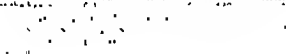


Fig 8 Abscissae x , ordinates probability density function $f(x)$ and probability $F(x)$

In probability distributions such as those of Figure 8, x is a continuous random variable [cf. (343)], there is an infinite number of events x_i , so that

$$\text{Prob}(x = k) = 1/\infty = 0 \quad (398)$$

and

$$\text{Prob}(x \leq k) = \text{Prob}(x < k) + \text{Prob}(x = k) = \text{Prob}(x < k) + 0$$

In practice therefore the following should be noted.

For continuous distributions (with an error of zero magnitude)

$$\left. \begin{aligned} \text{Prob}(x \leq k) &\text{ can be written as } \text{Prob}(x < k) \\ \text{Prob}(x \geq k) &\text{ can be written as } \text{Prob}(x > k) \end{aligned} \right\} \quad (399)$$

In discrete distributions the individual probability $\text{Prob}(x = k)$ can be read from $f(x)$ but this no longer applies in continuous distributions

In a continuous distribution, $f(x)$ is the *probability density function* at the point x .

$$\left. \right\} \quad (400)$$

The cumulative probability distribution $F(x)$ has the same significance in continuous distributions, however, as in discrete distributions* it represents the probabilities of the events $x \leq k$. In contrast to the case with discrete distributions, the latter are equivalent to the events $x < k$ [cf. (399)]

$$\left. \right\} \quad (401)$$

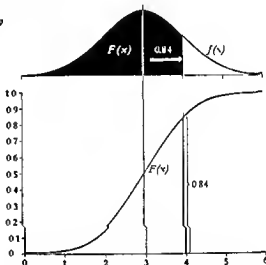
In discrete distributions, $F(x)$ is the *sum* of the individual probabilities [cf. (372)]. In continuous distributions, $F(x)$ is an *integral*

$$\left. \right\} \quad (402)$$

$$F(x) = \int_{-\infty}^x f(x) dx$$

i.e., $F(x)$ corresponds to the area between the abscissa and the curve $f(x)$ from $-\infty$ to x

Fig 9



The total area between the abscissa and the curve $f(x)$ from $-\infty$ to $+\infty$ amounts to unity [cf. (352)]

$$\left. \right\} \quad (403)$$

$$F(\infty) = 1, F(-\infty) = 0$$

$$F(\infty) = 1$$

Fig 10



For continuous distributions the equations analogous to (370)-(375) are the following

$$\text{Prob}(x = k) = 0, \text{ cf. (352) and (398)}$$

$$\text{Prob}(x \neq k) = 1, \text{ cf. (352)} \quad (404)$$

$$\text{Prob}(x \leq k) = \text{Prob}(x < k)$$

$$\left. \right\} \quad (405)$$

$$= \int_{-\infty}^k f(x) dx = F(k) \quad (a)$$


$$= 1 - \int_k^{\infty} f(x) dx \quad (b)$$

$$\text{Prob}(x \geq k) = \text{Prob}(x > k)$$


$$\left. \right\} \quad (406)$$

$$= 1 - \int_{-\infty}^k f(x) dx = 1 - F(k) \quad (a)$$

$$= \int_k^{\infty} f(x) dx \quad (b)$$



$$\left. \begin{aligned} \text{Prob}(k \leq x \leq r) &= \int_k^r f(x) dx = \int_{-\infty}^r f(x) dx - \int_{-\infty}^k f(x) dx \\ &= F(r) - F(k) \\ &= 1 - \int_{-\infty}^k f(x) dx = 1 - \int_{-\infty}^r f(x) dx \\ &= \int_k^{\infty} f(x) dx \end{aligned} \right\} \quad (407a) \quad (b) \quad (c)$$



$$\left. \begin{aligned} \text{Prob}(x < k) + \text{Prob}(x > r) &= 1 - \int_k^r f(x) dx = 1 - \int_{-\infty}^r f(x) dx + \int_{-\infty}^k f(x) dx \\ &= 1 - F(r) + F(k) \\ &= \int_{-\infty}^k f(x) dx + \int_r^{\infty} f(x) dx \\ &= 1 - \int_k^r f(x) dx \end{aligned} \right\} \quad (408a) \quad (b) \quad (c)$$

In equations (405)–(408), comparison with (399) shows for example that $\text{Prob}(k \leq x \leq r)$ is the same as $\text{Prob}(k < x \leq r)$, $\text{Prob}(k \leq x < r)$ and $\text{Prob}(k < x < r)$.

The numerical values of the various integrals in (405)–(408) for the most important distributions will be found in the statistical tables on pages 28 onward. They will be discussed further under the headings of the individual distributions later in this chapter. In the examples below in which probabilities in the normal distribution are calculated, the abscissae x are designated deviations e . In the table on page 28, $F(e)$ values are tabulated on the right (deviation \rightarrow integral), i.e., the probabilities $F(e)$ for given deviations e . On the left (integral \rightarrow deviation) are deviations e for given probabilities, so that here the deviation e is a function of $F(e)$, known as the quantile e (cf. section 10 E, page 160). Such a function is known as an *inverse function*. Tables of inverse functions are useful but not absolutely necessary. The values required can also be obtained from tables of basic functions by interpolation.

Example 14. The probabilities for $k = -1.65$ and $r = 1.96$ are calculated for the normal distribution using the form (a) of equations (405) to (408).

The right-hand side of the table on page 28 gives $F(-1.65) = 0.04947$ and $F(1.96) = 0.97500$, so that

$$(405): \text{Prob}(e \leq -1.65) = 0.04947$$

$$(406): \text{Prob}(e \geq -1.65) = 1 - 0.04947 = 0.95053$$

$$(407): \text{Prob}(-1.65 \leq e \leq 1.96) = 0.97500 - 0.04947 = 0.92553$$

$$(408): \text{Prob}(e \neq -1.65 \text{ to } 1.96) = 1 - 0.97500 + 0.04947 = 0.07447$$

Example 15. Given the probabilities $F(e) = 0.001$ and 0.995 it is required to find the corresponding deviations e . The left-hand side of the table on page 28 gives $e = -3.0902$ and 2.5758 . The corresponding values taken from the right-hand side without interpolation are 3.09 and 2.58 .

Example 16

Confidence intervals* and significance limits
(Cf. also sections 8 and 9, pages 154–159)

A. One-sided significance limits

Given α , where $0 < \alpha \leq 0.5$, determine x_1 and x_r in such a way that

$$\text{Prob}(x < x_1) = P_1 = \int_{-\infty}^{x_1} f(x) dx = F(x_1) = \alpha \quad (409)$$

$$\left. \begin{aligned} \text{Prob}(x > x_r) &= P_r = \int_{x_r}^{\infty} f(x) dx = 1 - \int_{-\infty}^{x_r} f(x) dx \\ &= 1 - F(x_r) = \alpha \end{aligned} \right\} \quad (410)$$

$$\text{From (410) it follows that } F(x_r) = 1 - \alpha \quad (411)$$

For the normal distribution, the table on page 28, left-hand side, gives for $\alpha = 0.025$, $x_1 = -1.96$ and $x_r = 1.96$.

The definitions of the symbols α , P_1 , P_r , x_1 and x_r in (409) and (410) are the same as in (378), (379) and (380).

It will be noted, however, that in contrast to discrete distributions [cf. (384)], the actual and nominal significance probabilities in continuous distributions are of the same magnitude. In continuous distributions therefore, the simple expression 'significance probability' is used, the symbols P and α becoming synonymous.

As in the case of discrete distributions it follows that:

If x attains or exceeds (to the left) the left (lower) significance limit x_1 , then in a one-tailed test

$$\text{Prob}(x \leq x_1) \leq \alpha = \text{Prob}(x < x_1)$$

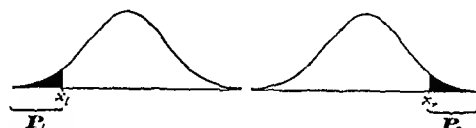


Fig. 11. One-sided significance limits for continuous distributions.

If x attains or exceeds (to the right) the right (upper) significance limit x_r , then in a one-tailed test

$$\text{Prob}(x \geq x_r) \leq \alpha = \text{Prob}(x > x_r)$$

The following definitions should also be noted:

The range between x_1 and ∞ or between $-\infty$ and x_r is the one-sided confidence interval.



Fig. 12. One-sided confidence intervals for continuous distributions.

x_1 and x_r are the one-sided confidence limits when the other limit lies at ∞ and $-\infty$ respectively. Again, significance limits and confidence intervals for continuous distributions are determined according to the same mathematical principles.

B. Two-sided significance limits

When a left and a right significance limit are jointly determined for a continuous distribution according to rules (409) and (410), then for the two together $P_1 + P_r = 2P = 2\alpha$.

In this case

$$2P = 2\alpha \text{ is the two-sided significance level.} \quad (411)$$

x_1 and x_r together are the two-sided significance limits, or briefly the significance limits.



Fig. 13. Two-sided significance limits for continuous distributions.

It should be noted:

If x attains or exceeds (outwards) one of the two significance limits x_1 or x_r , then in a two-tailed test

$$\left. \begin{aligned} \text{Prob}(x \leq x_1) + \text{Prob}(x \geq x_r) &\leq 2\alpha \\ \text{Prob}(x < x_1) + \text{Prob}(x > x_r) &= 2\alpha \end{aligned} \right\} \quad (420)$$

The following definitions should also be noted:

The range between x_1 and x_r is the two-sided confidence interval, or briefly the confidence interval.



Fig. 14. Two-sided confidence interval for continuous distributions

* Also known as 'tolerance intervals'. Cf. section 8, page 154.

c_1 and x_2 are the *two-sided* confidence limits (with symmetrical probability), or briefly the *confidence limits*. (422)

The probability $1 - 2P = 1 - 2\alpha$ is the *two-sided* confidence probability, or briefly the *confidence probability*:

$$\begin{aligned} \text{Prob}(x_1 \leq x \leq x_2) &= 1 - 2P \\ &= 1 - \int_{x_1}^{x_2} f(x) dx - \int_{x_2}^{x_1} f(x) dx = \int_{x_1}^{x_2} f(x) dx \\ &= \int_{x_1}^{x_2} f(x) dx - \int_{x_2}^{x_1} f(x) dx = F(x_2) - F(x_1) = 1 - 2\alpha \end{aligned} \quad (423)$$

7. Estimates

The variables of a population are usually known but not always the type of distribution and rarely the parameters, so that the distribution or its parameters must be estimated on the basis of samples. Estimates can be calculated from a sample using the same rules as for calculating the corresponding parameter of the population. This method of estimating is frequently used but it is not the only one and does not always give the best estimate.

unnecessary in practice since for the commonest cases a recognized estimating formula can be used.

7A. Expectation and bias

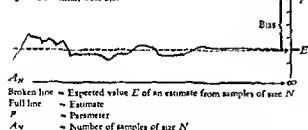
It is assumed that an estimate of some parameter P from a sample of size N is required

Experience has shown that when a number of similar estimates are made from samples of the *same* size the mean of these estimates approaches closer and closer to a definite value — the *expected value* or *expectation* of the estimate — when the number of samples is increased toward infinity (cf. Fig. 15). (424)

This convergence, however, is not a convergence in the usual mathematical sense but a *convergence in probability* or *stochastic convergence*, i.e., the probability that the convergence is arbitrary or zero (cf. (427)).

When the expectation of an estimate is equal to the parameter, the estimate is said to be *unbiased*. When this is not the case, the estimate has *bias*. (425)

Fig. 15 Estimation with bias



The bias can be dependent on the size of the sample. As a rule it is largest with small samples and tends toward zero when the sample size N approaches infinity. Such estimates are known as *asymptotically unbiased* estimates (cf. Fig. 16). (426)

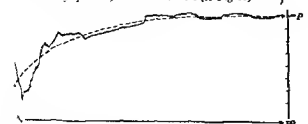


Fig. 16 Asymptotically unbiased estimation

* Higher from the standpoint of the non-mathematician

The bias described above is a mathematical one, that is, one inherent in the estimation. If the magnitude of this 'internal' bias is known, it can be eliminated by appropriate corrections*. An estimate can also have a non-mathematical, 'external' bias, however due to errors of measurement or judgment, to nonrandom selection of samples, or to both these causes. Such a bias is not

7B. Consistency

As in (424), experience has shown that with increasing sample size, estimates also usually tend toward a definite value, the *expected value* in *infinitely large* samples:

If with increasing sample size N a parameter remains constant, then
 Prob (| estimate minus expectation | $< \epsilon$) $\rightarrow 1$ ($\epsilon > 0$), as the sample size $N \rightarrow \infty$ (a)
 (a) is also valid for parameters that with increasing sample size N increase in proportion to N , N^2 , etc. when the absolute value of the difference between estimate and expected value is divided by N , N^2 , etc. (b)

7C. Efficiency

reader is referred to the original publications

Here the *most efficient estimate* is defined as that unbiased estimate of a parameter with variance equal to the lower bound of RAO-CRAMER. This will be assigned an efficiency of 100%.

Estimates fulfilling condition (429) for χ^2 tests, others not

Asymptotically most efficient estimates of (429) are suitable for χ^2 tests, others not

As a rule, the standard deviation of an estimate decreases absolutely or relatively (to the magnitude of the estimate) as sample size increases (cf. Fig. 17).

If a parameter remains constant with increasing sample size, the standard deviation of its estimate shows stochastic convergence toward zero of the order of $1/\sqrt{N}$ with increasing sample size N . (427)

* Corrections are not always possible when N is finite

(a) is also valid for parameters that with increasing sample size N increase in proportion to N , N^2 , etc. when the parameter, the estimate and its standard deviation are divided by N , N^2 , etc. } (b) (432)

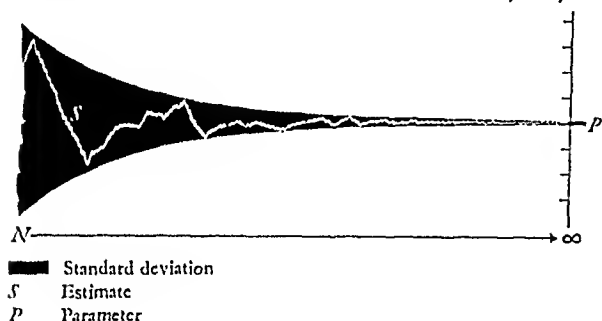
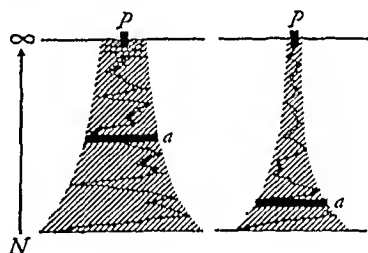


Fig. 17

If the efficiency of the estimate A is 100%, that of the estimate B for the same parameter 75%, then the sample size when using method B must be 100/75 times larger ($\frac{4}{3}$ as large again) than when using method A if the same degree of precision is to be obtained [provided that (432) applies]. (433)

Thus by increasing the size of the sample a less efficient estimate can be given the same precision as a more efficient one, (434)

or conversely, for a given degree of precision the sample size can be smaller when a more efficient method of estimation is used (cf. Fig. 18).

Fig. 18. a = precision of the estimate.

The question arises of which method to use in estimating a parameter when several formulae are available: that which yields the most efficient estimate but is more complicated, or a simpler but less efficient method? Theoretically, only the most efficient method should be used; in practice, however, the niceties of mathematical usage must be tempered by other considerations.

The most efficient of the known estimates of a parameter should be used

- when tests are expensive in comparison with simple counting [cf. (434)],
 - when the tests cannot be repeated,
 - when χ^2 tests are planned,
 - when the result must be as exact and informative as possible,
 - when the most efficient estimate has been used in similar studies by other investigators (thus offering the possibility of comparisons and significance tests).
- (435)

Where none of the reasons given in (435) apply, a less efficient but rapid method of estimating should be used

- when simple counting is more costly than the tests [cf. (434)],
 - when the precision of the method suffices for the purpose in mind,
 - when the object is simply a rapid preliminary check of the results,
 - when the investigations are of a routine nature,
 - when it is necessary to check more efficient estimates in the calculation of which there is a high possibility of error.
- (436)

7D. Sufficient estimates

An estimate or combination of estimates that in any given case yields all the information it is possible to obtain is known as a *sufficient estimate*. (4)

Information may be imagined (more or less) as the reciprocal of the variance. (4)

In conclusion it should be noted that as in the case of bias, the variance of an estimate is dependent on the experimental condition and can be reduced by suitable planning of the investigation.

The designations 'consistent', 'efficient' and 'sufficient' are due R. A. FISHER. However, FISHER reserves the term 'efficient' for the estimates described here as suitable for χ^2 tests [cf. (430) and (431)].

8. Confidence limits and tolerance limits

8A. Confidence limits for continuous and discrete distribution

In this subsection it is assumed that the reader is familiar with examples 13 and 16, pages 150 and 152.

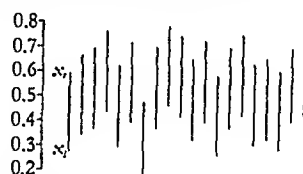
The estimation of a parameter alone does not yield a great deal of information. In a continuous distribution, for example, as (39) shows, the probability that the estimate $[x \text{ in } (398)]$ and parameter $[k \text{ in } (398)]$ agree is equal to zero. More information is provided by calculating from the sample the two values x_1 and x_2 that with a *high probability* enclose the parameter between them. Such limits are known as *confidence limits*. The associated terminology and mathematical definitions are given in examples 13 and 16 (pages 150 and 152).

The confidence limits used here are characterized as follows:

They are identical with the confidence limits of J. NEYMAN⁸. (439)

The parameter to which they relate is a *constant*. (440)

They are *estimates* and therefore *random variables*. Moreover, the *position of the limits* as well as the *width of the confidence interval* is a random variable (cf. Fig. 19). (441)

Fig. 19. 95% confidence intervals for the parameter P of a binomially distributed population, calculated from 20 samples of size 40.

For a given sample size, *more efficient* estimates result in a narrower confidence interval than less efficient ones. (442)

In analogy with (432), the confidence interval becomes absolutely or relatively (to the magnitude of the estimate) narrower with increasing sample size.

When a parameter remains *constant* with increasing sample size N , the confidence limits show stochastic convergence of the order of $1/\sqrt{N}$ toward the parameter and the width of the confidence interval shows stochastic convergence toward zero (cf. Fig. 20). (a) (443)

When the parameter is divided by N , N^2 , etc. and its confidence limits by N , N^2 , etc., (a) is also valid for parameters that with increasing sample size N increase in proportion to N , N^2 , etc. (b)

Confidence limits are to be interpreted as follows [see also (456)]: When very many (infinitely many) samples of the same size are taken from the same stable population and the confidence limits calculated for each, then these limits (*one-sided confidence intervals*)

- will enclose the true value of the parameter on the average in $\geq 100(1 - \alpha)\%$ of cases*
 - or (an equally valid interpretation)
 - will *not* enclose the true value of the parameter on the average in $\leq 100\alpha\%$ of cases*
- (a) (444)

* The 'greater than' and 'smaller than' signs apply to discrete distributions, the 'equals' sign to continuous distributions.

sided confidence intervals)

will enclose the true value of the parameter on the average in $\approx 100(1 - 2\alpha)\%$ of cases* (c)

in equally valid interpretation)

parameter (d)

a rule, the confidence probability 0.95 (more rarely 0.9) is used in medical and biological studies, α (one-sided intervals) or 2α (two-sided intervals) is equal to 0.05 or rarely 0.01 (445)

formulae for the calculation of confidence intervals for various

Fiducial limits. This concept, introduced by R. A. FISHER, strictly taking has a sense different to that of the *confidence limits* of NEYMAN. Fiducial limits can be precisely determined only for certain continuous distributions. For discrete distributions they can be determined approximately, but then only when the sample size is large. *Confidence limits* are not subject to these limitations and therefore are preferred here

3. Tolerance limits for continuous distributions

limits for a percentage of a population are known as tolerance limits (446)

the percentage of the population is expressed as $100\beta\%$, the confidence probabilities associated with tolerance limits as β_1 (447)

(446) and (447) are also valid for tolerance limits. (448)

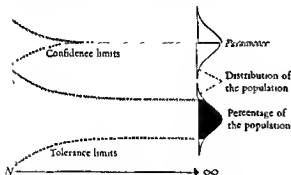


Fig 20 Convergence of confidence and tolerance limits

In analogy with (443), tolerance limits also converge stochastically with increasing sample size, but not toward one but toward two limiting parameters, namely those corresponding to the quantiles of the population between which lies the percentage of the population to which the tolerance limits relate. The tolerance interval between these limits thus tends not toward zero but toward a positive whole number (cf Fig 20) (449)

Like confidence limits, tolerance limits can be one- or two-sided. The following statements refer to two-sided tolerance limits in which

$$\beta_2 = 1 - 2\alpha, \text{ and } \alpha(\text{left}) = \alpha(\text{right}) = \int_{-\infty}^{\tau_1} f(x) dx = \int_{\tau_2}^{\infty} f(x) dx$$

Tolerance limits with confidence probability β_1 must be distinguished from those without. They are interpreted as follows [note also (456)]

* The 'greater than' and 'smaller than' signs apply to discrete distributions, the 'equals' sign to continuous distributions

Sample tolerance limits without confidence probability. When very many (infinitely many) samples of the same size are taken from the same stable population and the tolerance limits calculated each time, then these limits (a) (450)

– will enclose on the average $100\beta_1\%$ of the population or (an equally valid interpretation) (b) (450)

– will not enclose on the average $100(1 - \beta_1)\%$ of the population, whereby on the average $100\alpha\%$ of the population will lie below the left (lower) limit and $100\alpha\%$ above the right (upper) limit

Sample tolerance limits with confidence probability β_1 . When very many (infinitely many) samples of the same size are taken from the same stable population and the tolerance limits calculated each time, then these limits will include at least $100\beta_1\%$ of the population in an average of $100\beta_1\%$ of cases (451)

of a sample and a later single observation* (452)

Tolerance intervals with confidence probability [interpretation (451)] are wider than those without, as would be expected. With increasing sample size, however, both intervals converge toward the limiting interval of (499) (453)

present these have rarely been calculated precisely according to the rules for tolerance limits*. However, with the aid of the tables given in this book, their exact calculation will involve additional calculation only in a minimum number of cases

Normal ranges should therefore be determined in accordance with the rules for tolerance limits, and (a) (454)

– in general, as tolerance intervals without confidence probability [interpretation (450)] for $100\beta_1\% = 95\%$ of the population [cf (452)] (b) (454)

– in special cases (usually industrial, where for example the wastage must be kept as low as possible), as tolerance intervals with confidence probability β_1 [interpretation (451)]

In the above text the word 'normal' has been used – in 'normally distributed' and 'normal range' – in two different senses

Statements (444), (450) and (451) are correct only when the sample in fact originates from the population for whose parameter or percentage the limits were calculated*. The formulae for calculating these limits are specific for the individual types of population (455)

3C. Distribution-free confidence and tolerance limits (Cf also section 10F, page 161)

Statements (444), (450) and (451) are correct only when the sample in fact originates from the population for whose parameter or percentage the limits were calculated*. The formulae for calculating these limits are specific for the individual types of population (456)

If the type of distribution of a population is unknown, as is often the case, it is pointless – particularly with small samples – to calculate confidence and tolerance limits on the basis of assumptions concerning the distribution that are not justified by experience, the experimental conditions, and so on

* With large samples this is in any case pointless

In such cases the so-called *distribution-free* confidence and tolerance limits are used, provided that these are available for the case concerned. Statements (444), (450) and (451) are then valid *without any stipulation as to the distribution of the population**, i.e., they are valid for *all* populations with the sole provision that these are *continuous*. (457)

Distribution-free confidence and tolerance limits are *wider* than those calculated for populations of a specific type. This is understandable in view of the fact that they must satisfy (444), (450) and (451) for populations of widely differing kinds.

Distribution-free confidence limits for quantiles (median, quartile, percentile, etc.) of small samples (up to $N = 100$) of continuous populations can be read off *without* calculation from the tables on pages 104 et seq. An introduction to the calculation of distribution-free confidence and tolerance limits will be found, together with formulae, in sections 10F (page 161) and 20F (page 186).

The table of distribution-free tolerance limits on page 128 can be used to solve problems of the following type without the need of calculation: At the start of a series of tests it is often necessary to decide the size of the sample to be taken *when it is impossible to know the form of the population distribution*. On the one hand the sample must be large enough to be reasonably representative of the population, on the other hand not unnecessarily large and wasteful. The answer is provided by distribution-free tolerance limits and for most purposes these can be read off directly from the table mentioned. For example, if the two extreme values of the sample are to include 90% of the population with the high probability of 0.999, then the table gives a sample size of 88. In other words, if a sample of size 88 is taken, then with a probability of 0.999, 90% of the population will lie between the 1st and 88th values of the sample.

9. Statistical significance tests

9A. Introduction

With a 'true' die the probability of throwing the number 1, 2, ..., 6 is by definition exactly $1/6$, and the probability of throwing an even number is exactly $1/2$. In accordance with (331), the probability $1/2$ is a parameter of the population of events 'even number' and 'uneven number' produced by throwing the die.

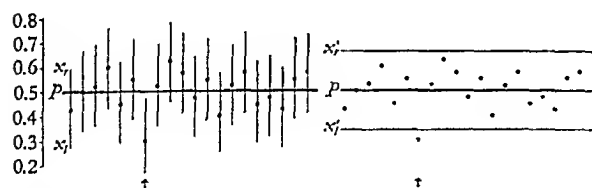


Fig. 21. 95% confidence limits (left) and corresponding 5% significance limits (right) for a given sample size (cf. legend of Fig. 19). The points are estimates \bar{p} of the probability $p = 1/2$ (shown here as the parameter P).

Such a die can be used to check statement (444d). 20 samples of 40 throws each are made and in each sample the uneven numbers thrown used to determine the 95% confidence limits given in Figure 21 (left) for the parameter $1/2$. In accordance with (444d), one of the 20 confidence intervals does not include the parameter (note arrow).

Supposing now that these confidence limits had been obtained not with samples consisting of *twenty throws of a known die* but with separate samples from *each of twenty unknown dice*. The suspicion would immediately arise that 'something was wrong' with that die for which the confidence interval did not include the parameter $1/2$. Only one sample has been thrown with this die, and in this first solitary sample a rare event occurs that according to (444d) should only occur in the long run in 5% of cases**. The suspected die is therefore declared to be loaded, but with the reservation that this assertion may err with a significance probability of 0.05.

This is the principle on which, *mutatis mutandis*, all statistical tests are based.

* Hence the expression 'distribution-free'.

** Further consideration will show that such an occurrence is possible, although with a much lower probability, since (444d) gives no indication when a rare event has to occur in a series of tests. With random events no such forecast can be made when the tests are independent.

9B. Significance limits

The example given above demonstrates that significance can be performed with the aid of confidence limits:

In a significance test based on *confidence or tolerance limits*, 1 or 2 *randomly variable limiting values* are compared with known or hypothetical *fixed parameter value* (cf. Fig. 21 left).

Many significance tests are performed with the aid of confidence limits:

In a significance test based on *significance limits* in the usual sense, 1 or 2 *constant limiting values* are compared with a *randomly variable test statistic* (cf. Fig. 21, right).

It is *immaterial* whether significance tests are made on the basis of confidence and tolerance limits or on the basis of significance limits in the usual sense: the result is the same (cf. Fig. 21, left and right). With both methods it is valid to deduce a significant difference [cf. (381), (382), (394), (413), (414) and (420)] *when the test statistic lies at or outside the limits*.

Confidence limits, tolerance limits and significance limits are intimately bound up with one another:

- either they differ from one another merely symbolically and are numerically identical } (a)
- or they differ in respect of formula and numerical value, with the formulae mutually interconvertible. } (b)

Example 17 [of (461a)]. In the binomial distribution

$$\begin{aligned} \uparrow \mathcal{P}_1 < p < \mathcal{P}_r & \text{ are significance limits for } p \\ \downarrow p_1 < \mathcal{P} < p_r & \text{ are confidence limits for } \mathcal{P} \end{aligned}$$

where \mathcal{P} are constants and p random variables. When, then $\mathcal{P}_1 = p_1$ and $\mathcal{P}_r = p_r$ (for the same sample size).

Example 18 [of (461b)]. \bar{x} is the mean, $s_{\bar{x}}$ the estimated standard deviation of the mean of a sample from a normally distributed population. μ_1 is the mean of the hypothetical population significance limit (corresponding to the sample size and significance probability) of the Student distribution (see 12A, page 166). Then

$$\begin{aligned} \bar{x} - t s_{\bar{x}} < \mu_1 < \bar{x} + t s_{\bar{x}} & \text{ are confidence limits for } \mu \\ - t s_{\bar{x}} < \bar{x} - \mu_1 < \bar{x} + t s_{\bar{x}} & \left\{ \begin{array}{l} \text{are neither confidence limits} \\ \text{significance limits in the} \\ \text{sense (like the test statistic)} \\ \text{limits are random variables} \end{array} \right. \\ - t < \frac{\bar{x} - \mu_1}{s_{\bar{x}}} < + t & \left\{ \begin{array}{l} \text{are significance limits for } \frac{\bar{x} - \mu_1}{s_{\bar{x}}} \end{array} \right. \end{aligned}$$

All three formulae are suitable for testing the null hypothesis $\mu_0 = \mu_1$ [see (466)]. This is done by replacing μ_1 by the hypothetical comparison parameter μ_0 and noting the position of the with regard to the limits. The simplest formula (for begin the first, the second allows the quickest calculation, while the is that most commonly used.

When the simple term 'limits' is used here in connection with significance tests [cf. (460) and (461) and their examples], then limits are meant which conform with rules (376) and (377) or (410), depending on the population under consideration.

All limits suitable for significance tests converge absolutely or relatively with increasing sample size or with increasing numbers of samples of the same size [when (432) holds]. The statements in (443) and (449) concerning confidence and tolerance limits are valid for all such limits.

It follows from (462) that:

- With increasing sample size, any difference existing can be demonstrated more and more significantly. } (a)
- With increasing sample size, smaller and smaller differences can be demonstrated for any given significance probability. } (b)

When there is a real difference — shown by small samples to be significant — between a real and a hypothetical population, then with increasing sample size the assumption that the real population *differs* from the hypothetical will be *confirmed* (usually) with increasing significance (cf Fig 22a).

When there is a real difference that *cannot* be shown

When there is in fact *no* difference between a real and a hypothetical population, then it *may* be possible to demonstrate this with some certainty with very large samples (with complete certainty only with infinitely large samples)

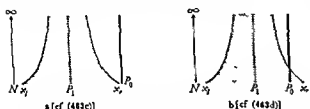


Fig 22a and b. P_1 is the hypothetical parameter, P_2 that to be tested, x_1 and x_2 are the confidence limits of P_1 converging with increasing sample size

9C. Significance tests

General

All statistical tests are based on the fundamental principle of comparing an *unknown* population from which the sample originates with a *known* or *hypothetical* population

All statistical tests confirm with precise significance probability only differences between the populations compared, *not* their identity [cf also (463)]

The hypothesis H_0 that 2 populations are identical is known as the *null hypothesis*. As implied in (463), it is usually postulated in order to be *disproved*

The expression null hypothesis is derived from the postulated identity of the population P_1 from which the sample originates with the hypothetical population P_2 , whence $P_1 = P_2$, so that $P_1 - P_2 = 0$ (null)

When a statistical test *“demonstrates”* a difference between

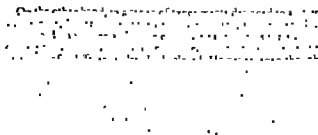
difference where none exists, is α or 2α

The probability of making an *error of the second kind*, i.e., of accepting the null hypothesis when it is untrue, in other words of not determining a difference where one exists, is β . The probabilities α and β are closely related: as α decreases β increases, and vice versa (note, however, that β is *not* $1 - \alpha$ or $1 - 2\alpha$, the reader is referred to more advanced statistical treatises for a detailed discussion of this relationship)

With increasing sample size it can be arranged that the probabilities of making an error of the first or second kind both decrease

Remarks on (467) and (468) When it is important to avoid making an error of the first kind, i.e., when it is necessary to be quite certain that a difference exists before accepting it, then a small value of α or 2α is chosen, say between 10^{-2} and 10^{-4} or less, according to the risk it is permissible to take

* In the subsequent text the word ‘test’ is used to mean ‘statistical test’



Power of a test

The probability $1 - \beta$, i.e., the probability of disclosing a difference when one actually exists, is known as the *power* of a test.

From (469) it follows that the power of a test can be increased (usually) by increasing the sample size

Remarks on (472) A useful analogy is that of the police searching for a criminal: the more that is known about him, the more effective (more powerful) will the search (the test) be

The *relative* power of different tests having the same object can only be decided by their use on *known* populations

Remarks on (473) The relative power of a test (previously calculated on the basis of some specific situation) is thus useless as a criterion for choosing between the two tests to be compared

Interpretations [cf also (476)]

When the purpose of a series of experiments is to demonstrate the *identity* of two populations, then the *failure* of an appropriate test to establish a significant difference justifies acceptance of the null hypothesis as long as it is not controverted by further experimentation

Remarks on (474) It is a common mistake to consider the identity of two populations as proven when no significant difference can be shown [cf also (463d and e) and Fig 22b]

When the purpose of a series of experiments is to demonstrate a difference between two populations

Remarks on (475) The interpretation ‘There is no difference’ would be incorrect [cf also (463d and e) and Fig 22b]

One-tailed and two-tailed tests

When from previous experience or on theoretical grounds the

* When α or 2α serves as a criterion of decision (rejection or acceptance of the null hypothesis), then the decision as to its magnitude must be made *independently* of the sample being tested, that is to say, if the investigator is in direct contact with the sample then *before* it is taken, if he is not in direct contact with it then *before* starting the statistical analysis

Interpretation of one-tailed tests*

Required significance	Test statistic		Interpretation and (in brackets) significance	
	Hypo- thetical	Test	One-tailed	Two-tailed
α	$x < x_1$	$\left\{ \begin{array}{l} x \leq x_1 \\ x > x_1 \end{array} \right.$	$x < x_1 (\leq \alpha)$ (475)	None
α	$x > x_r$	$\left\{ \begin{array}{l} x \geq x_r \\ x < x_r \end{array} \right.$	$x > x_r (\leq \alpha)$ (475)	

Interpretation of two-tailed tests*

2α	Uncertain	$\left\{ \begin{array}{l} x \leq x_1 \\ x \geq x_r \\ x_1 < x < x_r \end{array} \right.$	$\left\{ \begin{array}{l} x < x_1 (\leq 2\alpha) \\ x > x_r (\leq 2\alpha) \end{array} \right.$ (475) or (474)	Not equal (2 α)
-----------	-----------	------------------------------------------------------------------------------------------	-------------------------------------------------------------------------------------------------------------------	----------------------------

In general, however, particularly at the start of an investigation, there will be considerable doubt as to which of the populations is the smaller and which the larger, even if they can be distinguished at all. In this case a *two-tailed test* should be made. If no definite choice between a one- or a two-tailed test was made before sampling then no alternative to the latter test remains. The significance probability is 2α , conventionally 0.05 or 0.01**, i.e., $\alpha = 0.025$ or 0.005 [cf. remarks on (467) and (468)]. Note that even when the two-tailed test is interpreted as a one-tailed test, the significance probability of this interpretation is still 2α .

It should also be noted that the interpretation referred to here relates to the *test statistic*. The *real* interpretation based on this may be different. (476) is merely a summarized form of (381), (382), (392), (413), (414), (420), (474) and (475).

Conditions requiring fulfilment

It follows from (472) that in a situation in which several tests are available the one chosen will usually be that with the greatest power. According to (473), however, the choice is only possible when the form of the populations to be compared is known. The form may be known from *previous experience* or from *theoretical considerations* (game of chance, central limit theorem), or may be deduced from the sample itself when this is very large. When the sample is small, however, particularly in complex biological, medical or psychological studies, the form of the population is often unknown. In such cases, *assumptions* concerning the form are only too often made simply for the purpose of being able to apply a 'more powerful' test [which in actual fact it may not be; cf. (473)]. For the following reasons this should be avoided as far as possible:

In regard to the *reliability* of a statistical test result, it is wiser to risk losing a little of the information contained in the sample and to use a test contingent on fewer conditions and involving fewer assumptions or even none at all. A possibly more powerful test would require assumptions to be made that may result in illusory information not contained in the sample. (477)

When the conditions on which a test is based are not, or only partly, fulfilled, then the probabilities of making an error of the first or second kind are modified in a manner difficult to estimate. The one certainty is that the probabilities *valid* when the conditions are *fulfilled* are *no longer precise* or may be misleading when the conditions are not, or only partly, fulfilled. (478)

First of all therefore, in situations where several tests are available, care should be taken to choose a test in which (if possible) all the conditions it involves are *actually* fulfilled in the case under consideration. (479)

Situations are often encountered in which a choice according to (479) is impossible because in none of the available tests (sometimes there is only one) can all the conditions be fulfilled. In such a case the test result should be interpreted with a degree of *caution* depending on the effects the non-fulfilment of the conditions could have in the case con-

cerned. It is advisable to *specify the conditions which cannot be fulfilled*, for example as follows: 'On condition that both samples originate from the same normally distributed population, there exists...' (480)

It has already been stressed that the form of the population has an important bearing on the validity of many tests. In (477)–(480), however, conditions for tests are mentioned in a quite general sense. The number of conditions and their 'severity' varies from test to test: obviously as many as possible should be fulfilled and not only those concerned with the form of the population. One condition which is fundamental to *all* tests is the following:

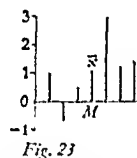
All statistical tests require that the samples should be *random* samples, that is to say, that they should be drawn by means of an operation fundamentally similar to that described in section 1, page 146. (481)

While this stipulation (481) is probably the most important condition in the whole field of statistics it is a very difficult one to fulfil completely in practice, especially in medical and biological studies. When an investigation has reached the stage of statistical testing, any nonrandom samples can probably be discarded provided that testing for nonrandomness is possible in the case concerned. Although this guards against making an erroneous decision, both time and money will have been wasted. For this reason it is advisable – *before* starting the investigation – to take all possible measures to ensure (maximum) randomness of sampling.

When as in (479) there are several permissible tests, no generally valid rules can be laid down as to how the choice should be made. Usually the first tests adopted will be those involving the least amount of calculation. If these do not give the postulated level of significance, they will be followed by more powerful tests from among those permissible. Such a procedure is in order* provided that it does not result in the mistake of assuming that a significance is doubly (or more than doubly) guaranteed when two (or more) tests give a significant result. The reason for this is that between many tests there exist correlations not always apparent even to the statistician: to some extent they test in the same manner but with different degrees of acuity. An analogy is provided by the viewing of an object under the microscope at three different magnifications: one is unlikely to fall into the error of assuming that its existence is triply confirmed. Similar but less easily recognizable relationships hold for tests between which there are correlations.

Example 19. Given the sample (in chronological order)

1 hour
– 0.7 hour
0.5 hour Mean $\bar{x} = 1.07$ hour
1.1 hour Median $M = 1.1$ hour
3 hours
1.2 hour
1.4 hour



representing the differences between pairs of observations on the same subject, for example after the administration of two barbiturates. The question is whether these differences differ significantly from zero ($2\alpha = 0.05$).

In such a case the following 7 tests are available (these are all given in the statistical tables preceding this chapter with the exception of the maximum test, for which the significance limits can be memorized):

Test	Stipulation regarding form of population	Calculation involved
1 Student (<i>t</i> -test)	Normally distributed	Among these tests the most About 1/4 of that in 1 Less than in 2
2 LORD		
3 Midrange (WALSH)		
4 WALSH	Symmetrical	About the same as in 2
5 Sign	None	None
6 Maximum (WALTER)	None	Arrangement only
7 WILCOXON	None	About the same as in 2

If it is known that the sample is from a normally distributed population, then *all* of these tests can be tried. In this case the

* For discrete distributions $x < x_1 + 1$ and $x > x_r - 1$ are used.

** See page 157, right-hand column, footnote.

* The editors know of no precise indications in this respect.

is powerful is the Student test, followed by the **LOD** and mid-range tests, which are only slightly less powerful with samples of small size. For normally distributed populations the **WILCOXON** is also little inferior to the Student test. If nothing is known of the form of the population, then tests 5, and 7 must be used, in accordance with (479). In the event of any of all these only the interpretation given in (473) remains. In the above example the tests yield the following significances—

Test	Significance
Student.....	$0.025 < 2\alpha < 0.05$
LOD.....	$0.05 < 2\alpha < 0.1$
Midrange.....	$0.05 < 2\alpha < 0.1$
WALSIT.....	—
Sign.....	$0.05 < 2\alpha$
Maximum.....	$0.05 < 2\alpha < 0.1$
WILCOXON.....	$2\alpha < 0.05$

The Student, midrange and WILCOXON tests yield the desired significance while the others more or less fail. This reflects the fact that when two samples are to be tested with respect to a difference in location between their populations, then as a rule for normally

The standard deviation is a measure of the variance. The smaller it is, the steeper the curve of the distribution, the larger it is, the flatter the curve (cf. Fig. 25). This relationship is the basis of the **CHEBYSHEV** inequality.

$$\text{Prob}(|x - \mu| \geq k\sigma) \leq 1/k^2 \approx 2\alpha \quad (k > 1) \quad (486)$$

and 10 This inequality is valid for any population

10B. Transformations

If the variable x is subject to a constant increment a , then

$$\left. \begin{aligned} X &= x \pm a \\ \text{so that} \\ \mu_X &= \mu_x \pm a \\ \sigma_X^2 &= \sigma_x^2 \end{aligned} \right\} (a) \quad (487)$$

The inverse transformation is

$$\left. \begin{aligned} \mu_x &= \mu_X \mp a \\ \sigma_x^2 &= \sigma_X^2 \end{aligned} \right\} (b)$$

The variance is unaffected by a lateral displacement, i.e., it is translation-invariant.

If the variable x is increased or decreased by a constant factor a , then

$$\left. \begin{aligned} X &= ax \\ \text{so that} \\ \mu_X &= a\mu_x \\ \sigma_X^2 &= a^2\sigma_x^2 \end{aligned} \right\} (a) \quad (488)$$

The inverse transformation is

$$\left. \begin{aligned} \mu_x &= \mu_X/a \\ \sigma_x^2 &= \sigma_X^2/a^2 \end{aligned} \right\} (b)$$

(487) and (488) are also valid for the estimates \bar{x} , \bar{X} and s_x , s_X of μ_x , μ_X and σ_x , σ_X , the calculation of which they often render easier.

Example 20

(a) Given

$x = 145 \ 145.5 \ 147 \ 147.3$ Then with $X = x - 145$
 $X = 0 \ 0.5 \ 2 \ 2.3$ from which values \bar{X} and s_X^2 are calculated, when

$$\bar{x} = \bar{X} + 145 = 1.2 + 145 = 146.2 \quad [\bar{X} \text{ from (491)}]$$

$$s_x^2 = s_X^2 = 1.26 \quad [s_X^2 \text{ from (493)}]$$

(b) Given

$x = 0.00325 \ 0.00160 \ 0.00320$ Then with $X = 10^4 x$
 $X = 325 \ 160 \ 320$ from which values \bar{X} and s_X^2 are calculated, when

$$\bar{x} = \bar{X}/10^4 = 268.3 \times 10^{-4} = 0.002683 \quad [\bar{X} \text{ from (491)}]$$

$$s_x^2 = s_X^2/10^8 = 8808.3 \times 10^{-8} = 8.8083 \times 10^{-4} \quad [s_X^2 \text{ from (493)}]$$

A variable x whose distribution has

$$\left. \begin{aligned} \text{mean} &= 0 \\ \text{and variance} &= 1 \end{aligned} \right\} (489)$$

is known as a *standardized variable*, or variable in *standard measure*.

If a variable x has the mean μ and the variance σ^2 , then the variable

$$X = \frac{x - \mu}{\sigma} \quad (490)$$

is in standard measure.

From the standardized variable X the original variable

$$x = \sigma X + \mu \quad (b)$$

is obtained

(489) and (490) are in common use in statistics

10C. Estimates of μ and σ based on ungrouped samples

The *most efficient, unbiased* estimate of the mean μ based on a sample from a normal population with the values x_1, x_2, \dots, x_N is

estigation by further experiment

Common rules in statistical testing

Division of the sample values in example 19 above by 10 leaves the significances resulting from the tests unchanged. This would result in a statistically 'guaranteed' difference in the action of the

is often happens that $\bar{x} = \bar{X} = 146.2$

10. Parameters

Means, variances and quantiles are dealt with only in a general manner in this section. Special formulae for calculating means and variances of various distributions are given in the sections dealing with these distributions.

10A. Mean and variance of the population

$$\left. \begin{aligned} \mu_x &= \frac{1}{N} \sum_{i=1}^N x_i \\ \sigma_x^2 &= \frac{1}{N} \sum_{i=1}^N (x_i - \mu_x)^2 \end{aligned} \right\} (482)$$

$$\left. \begin{aligned} \text{The square root of the variance is known as the } & \text{standard} \\ \text{deviation } (\sigma) & \end{aligned} \right\} (483)$$

$$\left. \begin{aligned} \text{The variance and standard deviation of the mean are} & \\ \text{expressed respectively by } \sigma^2/N \text{ and } \sigma/N \text{ and given the sym-} & \\ \text{bols } \sigma_x^2 \text{ and } \sigma_x & \end{aligned} \right\} (484)$$

$$\left. \begin{aligned} \text{The quotient } \sigma/\mu \text{ is known as the coefficient of variance } V & \\ \text{It is therefore the standard deviation with the mean ex-} & \\ \text{pressed as unity. } V \text{ has meaning only for positive values of } x & \end{aligned} \right\} (485)$$

$$\bar{x} = \frac{x_1 + x_2 + \dots + x_N}{N} = \frac{\sum x}{N}$$

(\bar{x} is read as 'x bar').

The most efficient, unbiased estimate s^2 of the variance σ^2 is

(a) when μ is known

$$s^2 = \frac{\sum (x - \mu)^2}{N} = \frac{S'_x}{N}; \text{ for } S'_x \text{ see (493a and b)} \quad (a)$$

(b) when μ is unknown

$$s^2 = \frac{\sum (x - \bar{x})^2}{N - 1} = \frac{S_x}{N - 1}; \text{ for } S_x \text{ see (493)} \quad (b)$$

The calculation of S_x (this symbol should be noted) is facilitated by the use of the following sums:

$$\left. \begin{aligned} S_x &= \sum (x - \bar{x})^2 \\ &= \sum x^2 - N\bar{x}^2 \quad \text{for } S'_x \text{ write } \mu \text{ instead of } \bar{x} \\ &= \sum x^2 - \bar{x} \sum x \\ &= \sum x^2 - (\sum x)^2/N \\ &= s^2(N - 1) \end{aligned} \right\} \quad (493)$$

The most efficient asymptotically unbiased estimate of σ is s . In practice the bias of s can usually be neglected. Correction factors for eliminating this bias in samples from normally distributed populations are given on page 47. (494)

The most efficient unbiased estimate of σ^2 is s^2 is s^2/N , the most efficient asymptotically unbiased estimate of σ^2 is $s^2 = s^2/N$. Cf. also (494). (495)

Other estimates of σ will be dealt with later.

Example 21 [of (491)–(495)]. Given the sample of example 19, page 158,

then according to formula (491) $\bar{x} = 7.5/7 = 1.0714$

$$(493) S_x = 15.35 - 8.0357 = 7.3143$$

$$(492) s^2 = 7.3143/6 = 1.2190$$

$$(494) s = \sqrt{1.2190} = 1.1041$$

$$(495) s_{\bar{x}} = 1.1041/\sqrt{7} = 0.4173$$

The results should finally be rounded off to a few decimal places in order not to imply an accuracy the estimates do not possess.

10D. Estimates of μ and σ^2 based on grouped samples

Given the classes x_1, x_2, \dots, x_n with the same class width for all classes $d = x_{i+1} - x_i$ and the frequencies f_1, f_2, \dots, f_n ($N = \sum f_i$), a provisional mean \bar{x}' is chosen falling in one class. The classes are now numbered. \bar{x}' receives the number $z = 0$, the classes downwards receive the numbers $z = -1, -2, \dots$, the classes upwards the numbers $z = 1, 2, \dots$

Classes $\dots (\bar{x}' - 2) (\bar{x}' - 1) \bar{x}' (\bar{x}' + 1) (\bar{x}' + 2) \dots$

$z \quad \dots -2 \quad -1 \quad 0 \quad 1 \quad 2 \quad \dots$

Then

$$\bar{x} = \bar{x}' + d \frac{\sum f z}{N} \quad (496)$$

$$s^2 = \frac{d^2}{N - 1} \left(\sum (f z^2) - \frac{(\sum f z)^2}{N} \right) \quad (497)$$

SHEPPARD'S correction

In the grouping of the individual values into classes a small error arises as a result of the random choice of the individual values. This introduces a small error into the estimate of the variance that can be corrected by subtraction of $k = 0.083$ (i.e., of $1/12$) from the variance estimated in class units. This correction (SHEPPARD'S correction) can be dispensed with in the testing of differences for significance but is otherwise to be recommended.

$$\text{SHEPPARD'S correction: } s_{\text{corr}}^2 = s^2 - \frac{d^2}{12} \quad (498)$$

Example 22. Diameter of erythrocytes. Class width $d = 0.4$

Class	Frequency f	De- viation z	Frequency \times deviation fz	Frequ \times sq of devi $fz^2 = f$
5.6	5	-4	-20	8
6.0	78	-3	-234	70
6.4	144	-2	-288	57
6.8	479	-1	-479	47
$7.2 = \bar{x}'$	542	0	0	0
7.6	358	+1	+358	358
8.0	279	+2	+558	1114
8.4	99	+3	+297	891
8.8	15	+4	+60	240
9.2	1	+5	+5	25
	$\Sigma(f) = N = 2000$		$\Sigma(fz) = 257$	$\Sigma(fz^2) = 257$

$$\bar{x} = 7.2 + 0.4 \frac{257}{2000} = 7.251 \mu\text{m}$$

$$s^2 = 0.4^2 \frac{4467 - 33.0}{1999} = 0.4^2 \times 2.218;$$

$$s = 0.4 \sqrt{2.218} = 0.596 \mu\text{m without SHEPPARD'S correction}$$

$$s^2 = 0.4^2 (2.218 - 0.0833) = 0.4^2 (2.135);$$

$$s = 0.4 \sqrt{2.135} = 0.584 \mu\text{m with SHEPPARD'S correction}$$

10E. Quantiles of continuous distributions

Definition: In $p = F(x)$, x is known as the *quantile* (p), here given the symbol $Q(p)$ or x_p . Quantiles are thus the *inverse function* of $F(x)$; they are so-called parameters of position. The quantile has also been given the name *fractile*. On $F(x)$ see also (401) and (402).

The quantiles most commonly used are given special names:

Quantile	Probability p
Quantile.....	$0.25 \times n$ ($n = 1, 2, 3, 4$)
Median.....	0.5 ($= 2\text{nd quantile}$)
Decile.....	$0.1 \times n$ ($n = 1, 2, \dots, 10$)
Percentile.....	$0.01 \times n$ ($n = 1, 2, \dots, 100$)

Interpretation of a quantile (p) of a continuous population:
 100 $p\%$ of the population lie below the quantile
 100 $(1-p)\%$ of the population lie above the quantile. (50)

Example 23. See Figure 8 (quantiles and median of a normal distribution), page 151.

Estimation

(a) **Ungrouped samples.** The quantile $Q(p)$ of a population is estimated by calculating the corresponding quantile $Q(p)$ of a sample taken from it. The sample values x are arranged in order of magnitude [cf. (342)] and numbered serially, the smallest value receiving the number 1. These *order numbers* are known as the *ranks* of the sample values x , so that

$$x_1 < x_2 < x_3 < \dots < x_N$$

The quantile $Q(p)$ thus corresponds to the sample value with the rank $O(p)$:

$$O(p) = Np + 0.5 \left(\text{for } \frac{1}{N} \leq p \leq \frac{N-1}{N} \right) \quad (501a)$$

If $O(p)$ is a whole number, the quantile $Q(p)$ coincides with the sample value; if $O(p)$ is a fraction, the quantile (p) lies between the sample values with ranks adjacent to $O(p)$, i.e., between x_i and x_{i+1} . There would be little point in interpolating between these two values.

If the sequence of ordered sample values contains ties [cf. (346)] and $O(p)$ falls on or between the ranks of tied values, then $Q(p)$ is given the magnitude of these tied values provided that the number of such ties is small compared with the sample size. In samples with very many ties (few classes and high frequencies) there is no point in determining quantiles in accordance with (501a).

Geigy



brings
inflammation
under control

$$\bar{x} = \frac{x_1 + x_2 + \dots + x_N}{N}$$

(\bar{x} is read as ' \bar{x} bar'.)

The most efficient, unbiased est...

(a) when μ is known

$$s^2 = \frac{\sum (x - \mu)^2}{N} = \frac{S_x'}{N}; \text{ for}$$

(b) when μ is unknown

$$s^2 = \frac{\sum (x - \bar{x})^2}{N - 1} = \frac{S_x}{N - 1};$$

The calculation of S_x (this ...
by the use of the following ...

$$\left. \begin{aligned} S_x &= \sum (x - \bar{x})^2 \\ &= \sum x^2 - N\bar{x}^2 \end{aligned} \right\} \text{ for } S_x' \text{ w.} \\ &= \sum x^2 - \bar{x} \sum x \\ &= \sum x^2 - (\sum x)^2 / N \\ &[= s^2 (N - 1)]$$

The most efficient *asymptotically*
In practice the bias of s can us...
tion factors for eliminating th...
normally distributed popul...

The most efficient unbiased esti...
the most efficient asymptotically...
is $s_{\bar{x}} = s/\sqrt{N}$. Cf. also (494).

Other estimates of σ will be

Example 21 [of (491)–(495)]. C...
page 158,

then according to formula (491)

(493)

(492)

(494)

(495)

The results should finally be ...
in order not to imply an a...

10D. Estimates of μ and σ^2

Given the classes x_1, x_2, \dots, x_N
classes $d = x_{i+1} - x_i$ and the f_i .
a provisional mean \bar{x}' is chosen ...
now numbered. \bar{x}' receives the
wards receive the numbers $z =$
the numbers $z = 1, 2, \dots$

Classes ... $(\bar{x}' - 2)$ $(\bar{x}' - 1)$ \bar{x}'

z ... -2 -1 0

Then

$$\bar{x} = \bar{x}' + d \frac{\sum f z}{N}$$

$$s^2 = \frac{d^2}{N-1} \left(\sum (f z^2) - \frac{(\sum f z)^2}{N} \right)$$

CHIFFARD'S correction

Example 24. Given the ranked sample

1 175 176 176 177 178 179 180 181 182 184 186
2 3 4 5 6 7 8 9 10 11

186 193 195 200 207 218 235 268 356 441
12 13 14 15 16 17 18 19 20 21

required to find the 1st quartile, median and percentile (0.7) in
ordance with (501a)

$$Q(0.25) = 0.25 \times 21 + 0.5 = 5.75$$

[$Q(0.25)$ lies between 1.78 and 1.79]

$$O(0.5) = 0.5 \times 21 + 0.5 = 11$$

[$Q(0.5)$ = 1.86 (note the tie)]

$$O(0.7) = 0.7 \times 21 + 0.5 = 15.2$$

[$Q(0.7)$ lies between 2.00 and 2.07]

(b) Grouped samples. Given are the ranked classes x_1, x_2, \dots, x_n , with class width $d = x_{i+1} - x_i$, and class frequencies f_1, f_2, \dots, f_n , where $f_1 + f_2 + \dots + f_n = N$, a sample size

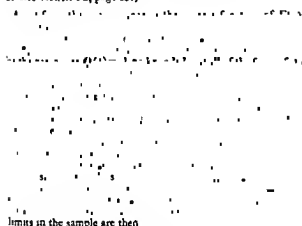
the cumulative frequencies are written as follows: $F_i = (1), f_1 + f_2 = F(2), f_1 + f_2 + f_3 = F(3)$, up to $f_1 + f_2 + \dots + f_n = F(n) = N$. Np is now compared with $F(i)$:

' $Np = F(i)$, then $Q(p) = x_i + \frac{1}{2}d$

' Np lies between $F(i)$ and $F(i+1)$, then $Q(p)$ lies between $x_i + \frac{1}{2}d$ and $x_{i+1} + \frac{1}{2}d$

10F. Distribution-free confidence limits for quantiles of continuous distributions

Cf also section 8C, page 135)



limits in the sample are then

$$\left. \begin{aligned} \text{for } p \leq 0.5 \quad O(p)_1 = x_1 + 1 \text{ and } O(p)_2 = x_p \\ \text{for } p > 0.5 \quad O(p)_1 = N - x'_p + 1 \text{ and } O(p)_2 = N - x'_1 \end{aligned} \right\} (502)$$

Example 25. For the sample in example 24 the 95% confidence limits are as follows

Quantile	Ranks		95% confidence limits
1st quartile	1 + 1 = 2	and 10	$176 < Q(p) < 184$
Median	5 + 1 = 6	and 16	$179 < Q(p) < 207$
Percentile (0.7)	21 - 12 + 1 = 10 and 21 - 1 = 20		$184 < Q(p) < 356$

10G. Relations between mode, median and mean of continuous distributions

The abscissa x of the maximum value of the density function $f(x)$ is known as the mode

In practice the mode is of little importance. On $f(x)$ see (499)

In one-peaked symmetrical distributions the mode, median and mean are coincident, but not in unsymmetrical distributions (cf Fig 31, page 165). The relationship between the three parameters is expressed by

$$\text{Median} \sim \frac{2}{3} \text{ mean} + \frac{1}{3} \text{ mode}$$

* In the case of large samples the time saved here will be offset by that lost in ranking the sample

Of main importance in practice is the identity of the median and the mean in symmetrical distributions: the distribution-free confidence limits for the median are valid also for the mean. It follows that

If the population mean \bar{x} of a sample coincides with either of the distribution-free confidence limits for the population median or lies outside them, then with a significance probability $\leq 2\alpha$, the sample does not originate from a symmetrical distribution (505)

This is the basis of the sign test, which is easily carried out and also independent of the form of the population

10H. The sign test

(a) Testing a sample for symmetry. \bar{x} is calculated, and the sample values, including \bar{x} , are ranked. The number $N(-)$ of sample values less than \bar{x} is counted and the test statistic S is calculated.

Example 26. In example 24 in section 10E, $\bar{x} = 2.130$, $N(-) = 16$. For $N = 21$ and $2\alpha = 0.05$, the table on page 105 gives the levels 5-16. With a significance probability of 0.05, the sample does not originate from a symmetrical distribution.

(b) Testing of pair differences (differences between pairs of observations).

Example 27. Of 500 pair differences, 210 are negative. Do the 500 differences differ on the average from zero ($2\alpha = 0.05$)? For $2\alpha = 0.05$ and $N = 500$ the table on page 105 gives the levels 227-273, so that the difference from zero is confirmed with the desired significance.

tion involved increases rapidly with increasing sample size). F differences can also be examined by sequential analysis (cf section 26, page 196).

11. The normal distribution

[Cf also section 6, page 151. For the meaning of 'normal' see (4)]

11A. Definition and characteristics

The normal distribution is a continuous distribution, the probability density function for which is defined by

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}\left(\frac{x-\mu}{\sigma}\right)^2} \quad (5)$$

(μ = mean, σ = standard deviation, for π and e see page 132)

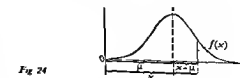


Fig 24

The curve of the probability density function

beings 9 feet tall or more should be 'possible'*. However, the word 'possible' is here inappropriate. 'Almost impossible' would be better, since the probability of extreme deviations from the mean decreases rapidly in the normal distribution.

If $\text{Prob}(|x - \mu| \geq k\sigma) \leq 2\alpha$, 2α changes with increasing k as follows†:

k	2α	k	2α
1	3.173105×10^{-1}	6	1.973175×10^{-9}
2	4.550026×10^{-2}	7	2.559625×10^{-12}
3	2.699796×10^{-3}	8	1.244192×10^{-15}
4	6.334248×10^{-5}	9	2.257177×10^{-19}
5	5.733031×10^{-7}	10	1.523971×10^{-23}

(507)

Remarks on (507): In accordance with the CHEBYSHEV Inequality [cf. (486)], the probability that in *any* distribution the variable x falls outside the limit $\mu \pm 3\sigma$, for example, is less than $1/9$; as (507) shows, however, in the normal distribution it is only $\sim 3/1000$. On the other hand, these much closer limits are valid *only* when the population is *in fact* normal. The inverse deduction should therefore also be noted, namely that should a distribution for which the 3σ limits are regarded as adequate *not* be normal, then the probability that the variable x falls outside these limits is *not* $3/1000$ but may be as large as $1/9$. This is an excellent illustration of (478).

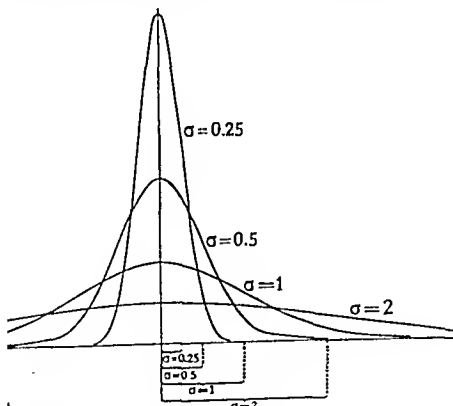
As with all symmetrical distributions, the mode, median and mean of the normal distribution are coincident. Their ordinate is the axis of symmetry of the curve of the probability density function [cf. Fig. 24 and (504)]. The most important consequences in practice are the following:

With a significance probability $\leq 2\alpha$, a sample that fails to pass the test for symmetry *does not* originate from a normally distributed population. (508)

If a *fairly small* sample passes the symmetry test [cf. also (474)], then the population from which it is drawn may still not be normal*. However, in significance tests (cf. page 158, 'Conditions requiring fulfilment') the stipulation of normality may be regarded as *almost* fulfilled. (509)

For *small* samples the sign test used for testing symmetry is relatively insensitive, that is, it will disclose an actual lack of symmetry in a population much more rarely with small samples than with large ones. For this reason (509) is valid only for *fairly small* samples. For small samples therefore, significance tests should be used – provided they are available – in which there are no conditions regarding symmetry or normality.

As (506) shows, the normal distribution is *fully* characterized by the two parameters μ and σ . The mean determines the *position* of the distribution with respect to the x axis, the standard deviation the *shape* of the curve: the larger σ is, the flatter the curve (cf. Fig. 25).



Distributions with various standard deviations.

For any values, the number of possible normal populations is infinite. If these are standardized

they appear illogical, limits according to probability are finite limits. The statement, for instance, that there is an height of the human body at, say, 8' 3", would manifestly

according to (490a), they are *all* *the* *same* *type* of normal distributions.

11B. The standardized normal distribution

If the quotient $(x - \mu)/\sigma$ in (490a) becomes the *standardized normal distribution* (standard deviation):

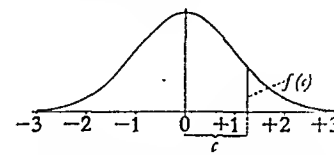


Fig. 26. Standardized normal distribution.

The symmetry of the distribution gives the following relationships:

Probability density function

$$f(0) = \max f(x) = 0.3989$$

$$f(-x) = f(x)$$

Probabilities

$$F(0) = \text{Prob}(x < 0) = \text{Prob}(x > 0) = 0.5$$

$$\text{Prob}(x < -k) = \text{Prob}(x > k)$$

$$= F(-k) = 1 - F(k)$$

$$\text{Prob}(-k \leq x \leq 0) = \text{Prob}(0 \leq x \leq k)$$

Quantiles

$$Q(1/2) = 0$$

$$Q(p) = -Q(1-p)$$

11C. Tables of the standardized normal distribution (pages 28–31)

Page	Table relates to	Left-hand side
28		Inverse function of the integral — = Quantile $Q(p)$ = $x(p)$ Argument p
29		Inverse function of the integral — = $x(p')$ Argument p'
30	Left-hand side Right-hand side 	$1 - \int_{-x}^x f(t) dt$ = $2P$ Argument x
31	Upper: ordinate $f(x)$, argument x . Cf. Fig. 26. Lower: inverse function of $1 - \int_{-x}^x f(t) dt$	

* For inverse function see page 31.

11D. Conversion of a normal distribution into the standardized form and vice versa (Cf. also section 10B, page 159)

The statement 'normal distribution with mean μ and standard deviation σ ' is here abbreviated to 'normal distribution'.

The normal distribution ($\mu; \sigma$) of the variable x is converted into the standardized normal distribution ($0; 1$) of the variable z (and vice versa) by substituting Z of (490) by z . (519)

In this conversion the probabilities of the converted values remain unchanged, so that (520)

$$\text{Prob}(x < x_0) = \text{Prob}(z < z_0)$$

Example 28. Given the normal distribution (174; 7), how large are the probabilities of the events $x < 160$, $x > 181$, $162 \leq x \leq 179$?

From (520)

$$\frac{160 - 174}{7} = -2, \quad \frac{181 - 174}{7} = 1, \\ \frac{162 - 174}{7} = -1.71, \quad \frac{179 - 174}{7} = 0.71$$

whence

$\text{Prob}(z < -2) = F(-2) = 0.02275$ (from the right-hand table on page 28)

$\text{Prob}(z > 1) = \text{Prob}(z < -1)$ [cf. (514a)] = 0.15866 (from the same table)

$\text{Prob}(-1.71 \leq z \leq 0.71) = \text{Prob}(-1.71 \leq z \leq 0)$, from (515),

$$= 0.4149 \times 7 + 174 = 162.4357$$

Example 29. Given the normal distribution of example 28, it is required to find

(a) the one-sided confidence limit x_1 for $1 - \alpha_1 = 0.95$

(b) the one-sided confidence limit x_2 for $1 - \alpha_2 = 0.99$

(c) the two-sided confidence limits x_1 and x_2 for $1 - 2\alpha = 0.95$

Solution:

All confidence limits or significance limits are quantiles (a)

(a) z_1 is the quantile (z_1), where $\alpha_1 = 1 - 0.95 = 0.05$. From the left-hand table on page 28, $z_1 = -1.6449$, whence $x_1 =$

$$-1.6449 \times 7 + 174 = 162.4357$$

(b) z_2 is the quantile (z_2), where $\alpha_2 = 1 - 0.99 = 0.01$. From the left-hand table on page 28, $z_2 = -2.3263$, whence $x_2 =$

$$-2.3263 \times 7 + 174 = 181.7119$$

and $x_2 = 1.960 \times 7 + 174 = 187.72$. Even simpler to obtain are the two-sided limits, namely from the left-hand table on page 29, using the deviation t , which can be read off directly by entering with the probability $1 - 2\alpha$

In connection with examples 28 and 29 it should be noted that, in practice, calculations are made with only as many decimal places as are required. However, it is advisable for beginners to complete the calculation with the full number of decimal places and then round off the result to the required number.

11E. The probit transformation

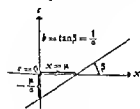


Fig 27a

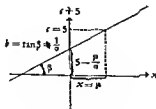


Fig 27b

The standardized variable $(x - \mu)/\sigma$ can be broken down in accordance with (34) into the fractions $-\mu/\sigma$ and x/σ . If $-\mu/\sigma = a$ and $1/\sigma = b$, then

$$z = a + bx, \text{ where } a = -\mu/\sigma \text{ and } b = 1/\sigma \quad (521)$$

In accordance with (299), the curve of (521) is a straight line (cf Fig 27a)

The straight line of (521) passes through the point $(\mu, 0)$. When μ and σ are known its construction therefore only requires one other point to be calculated from (521) (522)

If the straight line in Fig 27b is displaced 5 units in the direction of the ordinate axis, then

$$c + 5 = \text{prob} z = a + bx = 5 + b(x - \mu), \text{ whence} \\ a = 5 - b\mu \text{ and } b = 1/\sigma \quad (523)$$

The straight line of (523) passes through the point $(\mu; 5)$. When μ and σ are known its construction therefore only requires one other point to be calculated from (523) (524)

Since deviations of more than 5 σ are rare, the displacement 0 (521)–(523) means that in practice the majority of probit calculations are based on the straight line of (523).

Fig 27c: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

on samples

If the ordinate and abscissa scales are linear scales (cf. the

Fig 27d: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27e: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

distributed

If the abscissa axis is divided linearly and the ordinate

Fig 27f: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27g: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27h: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27i: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27j: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27k: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27l: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27m: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27n: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27o: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27p: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27q: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27r: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27s: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27t: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27u: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27v: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27w: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27x: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27y: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27z: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

11F. Fitting of normal curves to samples

Fig 27a: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27b: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27c: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27d: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27e: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27f: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

Fig 27g: A graph showing the transformation of a normal distribution curve into a straight line. The horizontal axis is labeled x and the vertical axis is labeled z. A straight line is drawn through the curve, with a point (x, z) marked. The slope of the line is indicated as b = tan phi = 1/sigma.

beings 9 feet tall or more should be 'possible'*. However, the word 'possible' is here inappropriate. 'Almost impossible' would be better, since the probability of extreme deviations from the mean decreases rapidly in the normal distribution.

If $\text{Prob}(|x - \mu| \geq k\sigma) \leq 2\alpha$, 2α changes with increasing k as follows¹⁰:

k	2α	k	2α
1	3.173105×10^{-1}	6	1.973175×10^{-9}
2	4.550026×10^{-2}	7	2.559625×10^{-12}
3	2.699796×10^{-3}	8	1.244192×10^{-18}
4	6.334248×10^{-4}	9	2.257177×10^{-19}
5	5.733031×10^{-7}	10	1.523971×10^{-23}

(507)

Remarks on (507): In accordance with the CHEBYSHEV Inequality [cf. (486)], the probability that in *any* distribution the variable x falls outside the limit $\mu \pm 3\sigma$, for example, is less than $1/9$; as (507) shows, however, in the normal distribution it is only $\sim 3/1000$. On the other hand, these much closer limits are valid *only* when the population is *in fact* normal. The inverse deduction should therefore also be noted, namely that should a distribution for which the 3σ limits are regarded as adequate *not* be normal, then the probability that the variable x falls outside these limits is *not* $3/1000$ but may be as large as $1/9$. This is an excellent illustration of (478).

As with all symmetrical distributions, the mode, median and mean of the normal distribution are coincident. Their ordinate is the axis of symmetry of the curve of the probability density function [cf. Fig. 24 and (504)]. The most important consequences in practice are the following:

With a significance probability $\leq 2\alpha$, a sample that fails to pass the test for symmetry *does not* originate from a normally distributed population. (508)

If a *fairly small* sample passes the symmetry test [cf. also (474)], then the population from which it is drawn may still not be normal**. However, in significance tests (cf. page 158, 'Conditions requiring fulfilment') the stipulation of normality may be regarded as *almost* fulfilled. (509)

For *small* samples the sign test used for testing symmetry is relatively insensitive, that is, it will disclose an actual lack of symmetry in a population much more rarely with small samples than with large ones. For this reason (509) is valid only for *fairly small* samples. For small samples therefore, significance tests should be used – provided they are available – in which there are no conditions regarding symmetry or normality.

As (506) shows, the normal distribution is *fully* characterized by the two parameters μ and σ . The mean determines the *position* of the distribution with respect to the x axis, the standard deviation the *shape* of the curve: the larger σ is, the flatter the curve (cf. Fig. 25).

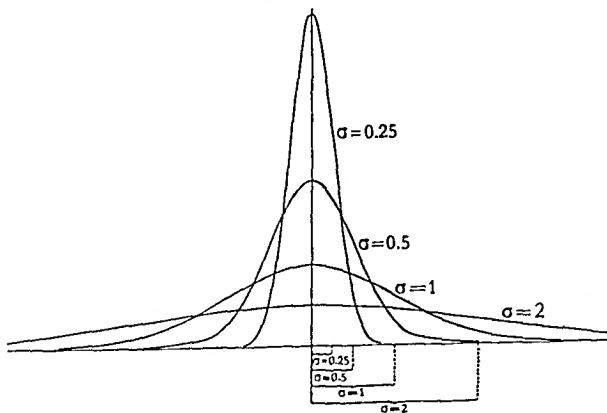


Fig. 25. Normal distributions with various standard deviations.

Since μ and σ can have any values, the number of possible normally distributed populations is infinite. If these are standardized

* Although they may appear illogical, limits according to probability are more logical than absolute limits. The statement, for instance, that there is an absolute limit to the height of the human body at, say, 8'3", would manifestly be untenable.

** Symmetrical distributions that are not normal also exist.

according to (490a), they are *all* transformed into *single* standardized normal distributions.

11B. The standardized normal distribution

If the quotient $(x - \mu)/\sigma$ in (490a) is denoted by ϵ , then (becomes the *standardized normal distribution* (with zero mean and standard deviation):

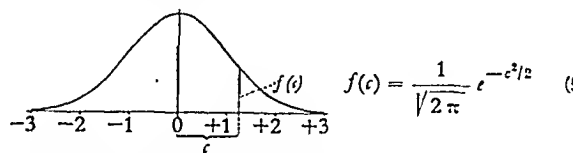


Fig. 26. Standardized normal distribution.

The symmetry of the distribution gives rise to the following relationships:

Probability density function

$$f(0) = \max f(\epsilon) = 0.398942 \quad (5)$$

$$f(-\epsilon) = f(\epsilon) \quad (5)$$

Probabilities

$$F(0) = \text{Prob}(\epsilon < 0) = \text{Prob}(\epsilon > 0) = \frac{1}{2} \quad (5)$$

$$\text{Prob}(\epsilon < -k) = \text{Prob}(\epsilon > k) \quad (a)$$

$$= F(-k) = 1 - F(k) \quad (b)$$

$$\text{Prob}(-k \leq \epsilon \leq 0) = \text{Prob}(0 \leq \epsilon \leq k) \quad (51)$$

$$\text{Quantiles} \quad Q(\frac{1}{2}) = 0 \quad (51)$$

$$Q(p) = -Q(1 - p) \quad (51)$$

11C. Tables of the standardized normal distribution (pages 28–31)

Page	Table relates to	Left-hand side	Right-hand side
28		Inverse function of the integral \rightarrow = Quantile $Q(p)$ = $\epsilon(p)$ Argument p	$\int_{-\infty}^{\epsilon} f(t) dt$ = $F(\epsilon) = p(\epsilon)$ Argument ϵ
29		Inverse function of the integral \rightarrow = $\epsilon(p')$ Argument p'	$\int_{-\epsilon}^{\epsilon} f(t) dt$ = $p'(\epsilon)$ Argument ϵ
30	Left-hand side: Right-hand side:	$1 - \int_{-\infty}^{\epsilon} f(t) dt$ = $2P$ Argument ϵ	$\int_{\epsilon}^{\infty} f(t) dt$ = $\int_{-\infty}^{\epsilon} f(t) dt$ Argument ϵ
31	Upper: ordinate $f(\epsilon)$, argument ϵ . Cf. Fig. 26. Lower: inverse function of $1 - \int_{-\infty}^{\epsilon} f(t) dt$		

* For inverse function see page 31.

11D. Conversion of a normal distribution into the standardized form and vice versa (Cf. also section 10B, page 159)

The statement 'normal distribution with mean μ and standard deviation σ ' is here abbreviated to 'normal distribution ($\mu; \sigma$)'. (518)

normal distribution (μ ; σ) of the variable x is converted into the standardized normal distribution (0, 1) of variable z (and vice versa) by substituting Z of (490)

(519)

is conversion the probabilities of the converted values in unchanged, so that

(520)

Example 28. Given the normal distribution (174; 7), how large are probabilities of the events $x < 160$, $x > 181$, $162 \leq x \leq 179$?

n (520)

$$\frac{60 - 174}{7} = -2, \quad \frac{181 - 174}{7} = 1,$$

$$\frac{62 - 174}{7} \sim -1.71, \quad \frac{179 - 174}{7} \sim 0.71$$

once

Prob ($z < -2$) = $F(-2) = 0.02275$ (from the right-hand table on page 28)

Prob ($z > 1$) = Prob ($z < -1$) [cf. (514a)] = 0.15866 (from the same table)

Prob ($-1.71 \leq z \leq 0.71$) = Prob ($-1.71 \leq z \leq 0$), from (515),

$$= \text{Prob} (0 \leq z \leq 1.71) - \text{Prob} (0 \leq z \leq 0.71) = 0.45984 - 0.25804 = 0.20180$$

Page 30).

Example 29. Given the normal distribution of example 28, it is required to find

- the one-sided confidence limit x_1 for $1 - \alpha_1 = 0.95$
- the one-sided confidence limit x_2 for $1 - \alpha_2 = 0.99$
- the two-sided confidence limits x_1 and x_2 for $1 - 2\alpha = 0.95$.

Solution

All confidence limits or significance limits are quantiles (z).

(a) z_1 is the quantile (z_1), where $\alpha_1 = 1 - 0.95 = 0.05$. From the left-hand table on page 28, $z_1 = -1.6449$, whence $x_1 = -1.6449 \times 7 + 174 = 162.4857$.

(b) z_2 is the quantile ($1 - \alpha_2$) = $Q(0.99)$. From the left-hand table on page 28, $z_2 = 2.3263$, whence $x_2 = 2.3263 \times 7 + 174 = 190.2841$.

(c) z is the quantile ($1 - 2\alpha$) = $Q(0.95)$. From the left-hand table on page 28, $z = 1.95996$, whence $x = 1.95996 \times 7 + 174 = 187.71972$.

For the two-sided limits, the deviation z can be read off directly by entering with the probability $1 - 2\alpha$.

Even simpler to obtain are the one-sided limits, namely from the left-hand table on page 29, using the deviation z , which can be read off directly by entering with the probability $1 - \alpha$.

In connection with example 28, it is also possible to find the probability of the event $160 \leq x \leq 179$.

From the left-hand table on page 28, $\text{Prob} (z \leq -1.71) = 0.0438$, and from the right-hand table on page 28, $\text{Prob} (z \leq 0.71) = 0.2580$.

Whence $\text{Prob} (-1.71 \leq z \leq 0.71) = 0.2580 - 0.0438 = 0.2142$.

11E. The probit transformation

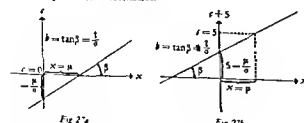


Fig 27a

Fig 27b

The standardized variable $(x - \mu)/\sigma$ can be broken down in accordance with (34) into the fractions $-\mu/\sigma$ and x/σ . If $-\mu/\sigma = a$ and $1/\sigma = b$, then

$$z = -bx + b\mu \quad (521)$$

Whence, the curve of (521) is a straight line (cf

The straight line of (521) passes through the point (μ ; 0). When μ and σ are known its construction therefore only requires one other point to be calculated from (521)

(522)

If the straight line in Fig 27b is displaced 5 units in the direction of the ordinate axis, then

$$z + 5 = \text{probit} = -bx + b\mu = 5 + b(x - \mu), \quad \text{whence} \quad (523)$$

The straight line of (523) passes through the point (μ ; 5). When μ and σ are known its construction therefore only requires one other point to be calculated from (523)

(524)

Since deviations of more than 5 σ are rare, the displacement of (521)–(523) means that in practice the majority of probit calculations can be carried out by means of the probit scale.

Figure 28 shows the probit scale and the scale of probability paper.

Figure 29 shows the probit scale and the scale of probability paper.

Figure 30 shows the probit scale and the scale of probability paper.

Figure 31 shows the probit scale and the scale of probability paper.

Figure 32 shows the probit scale and the scale of probability paper.

Figure 33 shows the probit scale and the scale of probability paper.

Figure 34 shows the probit scale and the scale of probability paper.

Figure 35 shows the probit scale and the scale of probability paper.

Figure 36 shows the probit scale and the scale of probability paper.

Figure 37 shows the probit scale and the scale of probability paper.

Figure 38 shows the probit scale and the scale of probability paper.

Figure 39 shows the probit scale and the scale of probability paper.

Figure 40 shows the probit scale and the scale of probability paper.

Figure 41 shows the probit scale and the scale of probability paper.

Figure 42 shows the probit scale and the scale of probability paper.

Figure 43 shows the probit scale and the scale of probability paper.

Figure 44 shows the probit scale and the scale of probability paper.

Figure 45 shows the probit scale and the scale of probability paper.

Figure 46 shows the probit scale and the scale of probability paper.

Figure 47 shows the probit scale and the scale of probability paper.

Figure 48 shows the probit scale and the scale of probability paper.

Figure 49 shows the probit scale and the scale of probability paper.

Figure 50 shows the probit scale and the scale of probability paper.

Figure 51 shows the probit scale and the scale of probability paper.

Figure 52 shows the probit scale and the scale of probability paper.

Figure 53 shows the probit scale and the scale of probability paper.

Figure 54 shows the probit scale and the scale of probability paper.

Figure 55 shows the probit scale and the scale of probability paper.

Figure 56 shows the probit scale and the scale of probability paper.

Figure 57 shows the probit scale and the scale of probability paper.

Figure 58 shows the probit scale and the scale of probability paper.

Figure 59 shows the probit scale and the scale of probability paper.

Figure 60 shows the probit scale and the scale of probability paper.

Figure 61 shows the probit scale and the scale of probability paper.

must be grouped, and the parameters μ and σ must be estimated by means of \bar{x} and s in accordance with (491) and (492) [cf. the remarks on these equations and also (430)]. In equations used in testing for goodness of fit, μ and σ are replaced by \bar{x} and s .

(a) Ungrouped samples

With ungrouped samples, empirical and fitted probit values can be compared only by eye. From (499) and (501a) it follows that

$$P_i = F(x_i) = \frac{O_i - 0.5}{N} \quad (527)$$

(O_i = rank of the individual sample value x_i ; cf. section 10E, page 160)

The empirical and fitted probits can then be calculated from (527) in conjunction with (523)–(525).

Example 30. Given is the sample of example 24, section 10E, page 161. The mean \bar{x} is 2.130, and the standard deviation s is 0.6713. The $F(x_i)$ values are first calculated according to (527): $F(x_1) = 0.5/21$, $F(x_2) = 1.5/21$, etc. [equation (31) is used here: $0.5/21 + 1/21 + \dots$]. By multiplying by 100, these values are converted into percentages, which are then used in the table on pages 54 and 55 to obtain the probits. For x_1, x_2, \dots this gives the empirical probits 3.0, 3.5, 3.8, 4.0, etc. These values are plotted on millimetre paper in accordance with (525) to give the result shown in Figure 29.

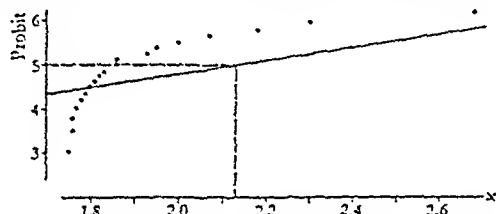


Fig. 29. Empirical probits and fitted probit line for the ungrouped sample of example 24, section 10E, page 161.

It will at once be seen that the points plotted deviate systematically from a straight line, indicating that it is very unlikely that the sample originates from a normally distributed population (as indeed was already clear from the result of the symmetry test of section 10H, page 161). If the sample had originated from a normal population, the points would have been distributed stochastically around the fitted probit line calculated in accordance with (523) and (524) from \bar{x} and s in place of μ and σ .

(b) Grouped samples

In this case

$$f(x_i) = \frac{Nd}{\sigma} f(\epsilon_i), \quad \epsilon_i = \frac{x_i - \mu}{\sigma} \quad (528)$$

$$F(x_i + \frac{1}{2}d) = \sum_{j=1}^i f_j / N \quad (529)$$

(i = ranks of the classes x_i , $d = x_{i+1} - x_i$ = class width, f_i = frequency of the class i)

If both the fitted probability density and the cumulative distribution are to be calculated, then $x_i + \frac{1}{2}d$ is also used in (528) and the calculated ordinates plotted against $x_i + \frac{1}{2}d$, that is to say, at the upper limit of the class i . (528) gives the ordinates for the middle of the classes.

Example 31. Given is the sample of example 22, section 10D, page 160, with $\bar{x} = 7.251$, $s = 0.584$.

Table 1

$x + \frac{1}{2}d$	$x + \frac{1}{2}d - \bar{x}$	$(x + \frac{1}{2}d - \bar{x})/s$	$f(\epsilon)$	$f(\epsilon) \times Nd/s = f(x + \frac{1}{2}d)$
5.4	-1.851	-3.17	0.00262	3.6
5.8	-1.451	-2.48	0.01842	25.2
6.2	-1.051	-1.80	0.07895	108.2
6.6	-0.651	-1.11	0.21546	295.2
7.0	-0.251	-0.429	0.36387	498.5
7.4	0.149	0.255	0.38618	529.0
7.8	0.549	0.939	0.25671	351.7
8.2	0.949	1.62	0.10741	147.1
8.6	1.349	2.31	0.02768	37.9
9.0	1.749	2.99	0.00457	6.3

Calculation of the fitted probability density

The calculation is made as follows: The differences $x_i + \frac{1}{2}d$ are multiplied by $1/s$ to obtain the fitted ϵ_i values [this can also be carried out as a simple addition by using equation (31)]. For the deviations ϵ_i , the corresponding ordinates $f(\epsilon_i)$ are obtained from the upper table on page 31 [in this connection see also (51)]. Multiplication of these ordinates by Nd/s gives the required ordinates $f(x_i + \frac{1}{2}d)$. (Cf. Fig. 30, left.)

Calculation of the empirical probits

The values of $F(x_i + \frac{1}{2}d)$ are calculated from (529), multiplied by 100, and the table on pages 54 and 55 entered to obtain the corresponding probits. The latter are plotted against $x_i + \frac{1}{2}d$ ordinates, giving the points of Figure 30, right.

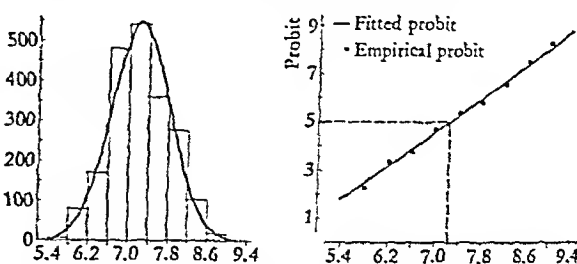


Fig. 30. Fitted probability density, empirical probits and fitted probit line for the sample of example 22 in section 10D, page 160.

Calculation of the fitted probit line

The probit line is constructed according to (524). In this example it first passes through the point (7.25; 5). If the value $x = 5.4$, say, is taken as the abscissa of the other necessary point, then from (523) the corresponding probit is $5 + 1.712(5.4 - 7.25) = 1.8$. When a straight line is drawn between these two points it is seen that the empirical probits all lie very close to it. The immediate impression given by Figure 30, right, is hardly such as to raise doubts that the population from which the sample is taken is other than a normally distributed one. That this impression is misleading, however, is demonstrated below.

Note that when the probability density is calculated as shown above, the two points required for the construction of the fitted probit line can be obtained by taking two remotely separated values from the column headed ϵ of Table 1 and increasing them by 5.

Exact testing for non-normality by the χ^2 test

In this case the test is carried out by means of the ϵ transformation, without probits, as follows (cf. Table 2 on page 165):

- For calculation of the fitted ϵ values for $x_i + \frac{1}{2}d$ according to (521) see column ϵ of Table 1, which contains these values.
- The $F(\epsilon)$ values corresponding to these fitted ϵ values are obtained from the table on page 28. These are the fitted $F(\epsilon)$ values.
- Multiplication of the fitted $F(\epsilon)$ values by the sample size N gives the fitted distribution of the cumulative absolute frequencies $H(x_i + \frac{1}{2}d)$.
- From the differences $H(x_{i+1} + \frac{1}{2}d) - H(x_i + \frac{1}{2}d)$, the fitted absolute class frequencies f_i^* are obtained.
- From these the values of $(f_i - f_i^*)^2/f_i^*$ are calculated.
- The sum of all the χ_i^2 values is the required test statistic χ^2 with degrees of freedom $v = n - 2 - 1$, where n = number of classes.

The significance probability 2α of the χ^2 value obtained (cf. the table on page 36) is considerably smaller than 0.0005. Hence the population from which the sample originates is definitely not normally distributed, a result completely contrary to the impression gained by eye from the empirical probits (above).

Note that in the above calculation the sequence of the signs of the differences $f_i - f_i^*$ should be looked at closely. The occurrence of pluses and minuses should vary randomly. If any systematic trend is detected, HALDANE's test (page 193) should be carried out, if there are systematic cycles, a test of randomness of runs (page 194) provided there are enough classes. The reason for this is that if the χ^2 test gives no significant result when the number of classes is large – as in the above example – then it can be assumed with reasonable certainty that the population is normally distributed provided that there is random variation of the plus and minus runs. If the latter is not the case then the χ^2 test needs supplementation. The test is also conditional on the classes being independent of one another. This is

Table 2

$x + \frac{1}{2}d$	$F(x)$	$F(x) \times N =$ $H(x + \frac{1}{2}d)$	$H(x_1 + \frac{1}{2}d)$ minus $H(x_1 + \frac{1}{2}d)$ $= f_i$	f_i [cf (381b)]	$(h - f_i^2)/K$ $= x_i^2$
5.4	0.00076	1.5	1.5*	5	5.01
5.8	0.00657	13.1	11.6	78	6.27
6.2	0.03593	71.9	58.8	144	13.38
6.6	0.13550	267.0	195.1	479	15.52
7.0	0.33360	667.2	400.2	542	0.05
7.4	0.60257	1205.1	537.9	358	17.97
7.8	0.82639	1652.8	447.7	279	5.66
8.2	0.94738	1894.8	84.3	99	2.56
8.6	0.98956	1979.1	18.1	15	0.53
9.0	0.99861	1997.2	2.8	1	1.16
9.4	—	—	2000.0	2009	$x^2 = 68.09$ $v = 10 - 2 = 1$ $= 7$

11G. Standard deviations of the quantiles of samples from normally distributed populations

The formulae given here are only asymptotically correct and better to use the procedure given in section 10F, page 161 (distribution-free confidence limits) and not calculate them by means of the standard deviations defined in the formulae given here

(Asymptotic)

$$\text{Standard deviation of } x_p = \sigma_{x_p} = \frac{1}{f(x_p)} \sqrt{\frac{p(1-p)}{N}} \quad (530)$$

From (530) and (504) it follows that

$$\text{Standard deviation of the median } \left\{ x_{.5} - \sigma_{x_{.5}} = \sigma \sqrt{\frac{\pi}{2N}} = 1.2533 \sigma \sqrt{\frac{1}{N}} \right. \quad (531)$$

In a normal distribution the median is identical with the mean μ . The median of a sample is therefore also an estimate of μ . The relative asymptotic efficiency of this estimate according to (433), (484) and (531) is

$$\frac{\sigma/\sqrt{N}}{\sigma/\sqrt{\pi/2N}} = \sqrt{\frac{2}{\pi}} \sim 0.8$$

that is to say, about 80% of the efficiency of the estimate of μ made from \bar{x} according to (491)

11H. The logarithmic-normal (lognormal) distribution

The probability density function of this distribution is

$$f(x) = \frac{0.4343}{x \times \sigma_{\log x}} \times f(z), \quad (532)$$

$$z = \frac{\log x - \mu_{\log x}}{\sigma_{\log x}}, \quad (0 < x < \infty)$$

The estimates of $\mu_{\log x}$ and $\sigma_{\log x}$ are $\bar{x}_{\log x}$ and $s_{\log x}$ calculated according to (491) and (492a and b) by substituting $\log x$ for x and $(\log x)^2$ for x^2

The logarithmic-normal distribution is unsymmetrical (cf Fig 31a) and has the following characteristics

$$\text{Mode} = \text{antilog}(\mu_{\log x} - 2.3026 \sigma_{\log x}) \quad (533)$$

$$\text{Median} = \text{antilog } \mu_{\log x} \quad (534)$$

$$\text{Mean} = \text{antilog}(\mu_{\log x} + 1.1513 \sigma_{\log x}) \quad (535)$$

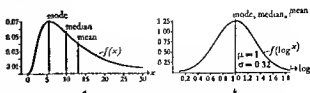


Fig 31 a Lognormal distribution b Transformation of a

If x is plotted on a logarithmic abscissa scale (or $\log x$ on a linear abscissa scale) the unsymmetrical distribution (532) is transformed into the symmetrical normal distribution

$$f(\log x) = \frac{1}{\sigma_{\log x}} \times f(z), \quad (536)$$

$$z = \frac{\log x - \mu_{\log x}}{\sigma_{\log x}}, \quad (0 < x < \infty)$$

[for $\mu_{\log x}$ and $\sigma_{\log x}$ see (532)]

From (532) and (536) it follows that

$$f(x) = \frac{0.4343}{x} \times f(\log x) \quad (537)$$

The probability density function of the transformed variable z is given by the normal distribution curve (536). The probability density function of the transformed variable z is given by the normal distribution curve (536).

$$F(x_p) = F(\log x_p) = p \quad (538)$$

$$\text{Similarly for the quantiles} \quad (539)$$

$$x_p = \text{antilog}(\log x_p) \quad (540)$$

and for ungrouped samples

$$O(x_p) = O(\log x_p) \quad (541)$$

(O = ranks of the individual sample values, cf section 10E, page 160)

From (538) and (539)–(540) it follows that [for (541)–(543)]

$$\text{The probability density function of the transformed variable } z \text{ is given by the normal distribution curve (536). The probability density function of the transformed variable } z \text{ is given by the normal distribution curve (536).} \quad (541)$$

If the transformation in (536) yields samples from a normally distributed population (cf (508) and section 11F, page 163), then any tests valid for the latter may be applied to these samples. The results of these tests will also be valid for the untransformed samples

For the estimation of the quantiles and their confidence

$$\text{For grouped samples the following should be noted: the transformation } x \rightarrow \log x \text{ may be carried out only with the individual values. If a sample is grouped into classes it must first be rearranged into an ungrouped sample. The logarithms of the individual values are then obtained.} \quad (542)$$

In natural processes many random variables are lognormally distributed. In all cases where the reaction of a body to a given stimulus is proportional to the intensity of the stimulus and to the

* The quantiles of a transformed variable are given by the transformed quantiles of the original variable provided that the transformation was made with an increasing function [if $\log x$ is an increasing function of x]

size of the body, the form of the distribution is lognormal. In practice, this applies particularly to toxicological and other similar biological studies, where logarithmic transformation of the variable X (dose) is a matter of routine.

11. The addition theorem for the normal distribution

If X_1, X_2, \dots, X_k are stochastically independent, normally distributed variables with mean values $\mu_1, \mu_2, \dots, \mu_k$ and variances $\sigma_1^2, \sigma_2^2, \dots, \sigma_k^2$, then the variable

$$X = X_1 \pm X_2 \pm \dots \pm X_k$$

is also normally distributed with mean

$$\mu = \mu_1 \pm \mu_2 \pm \dots \pm \mu_k$$

and variance

$$\sigma^2 = \sigma_1^2 + \sigma_2^2 + \dots + \sigma_k^2$$

(545)

In (545) it should be noted that the variances are also additive when the mean μ is obtained from differences.

11. The central limit theorem

The importance of the normal distribution lies in the fact that under fairly general conditions, the sum of k stochastically independent variables of any sort converges stochastically with increasing k toward a normal distribution with mean

$$\mu = \mu_1 + \mu_2 + \dots + \mu_k$$

and variance

$$\sigma^2 = \sigma_1^2 + \sigma_2^2 + \dots + \sigma_k^2$$

(546)

From (545) the sum of normally distributed variables is always normally distributed, even when k is small. (546) is valid for variables distributed in any form, however, only when k approaches infinity. In practice, the expression 'infinity' is interpreted liberally. Thus, if for example in (546) the distributions all have the same, not too unsymmetrical form, then practically speaking their sum is normally distributed even when k is fairly small (50, 100, 200, ...). In other words, there will be a negligible error if the sample distributions are treated as normal.

In this publication, the statistical tables relating to sample distributions are so arranged that samples exceeding the tabulated sizes can for practical purposes be regarded as normally distributed.

(547)

With one exception, all the sample distributions dealt with in this chapter converge toward the normal distribution in accordance with (546). The exception is the distribution of the extreme range and of course that of the extreme deviations).

2. Distributions closely allied to the normal distribution

2A. The Student distribution

If in the standardized normal deviation $t = (x - \mu)/\sigma$ the standard deviation σ has to be replaced by its estimate s because σ is unknown and thus has to be estimated from the sample, then the standardized variable

$$t_v = \frac{x - \mu}{s_v} \quad (s_v \text{ independent of } x) \quad (548)$$

as a probability density function

$$f(t|v) = \frac{\Gamma\left(\frac{v+1}{2}\right)}{\Gamma\left(\frac{v}{2}\right)\sqrt{v\pi}} \left(1 + \frac{t^2}{v}\right)^{-(v+1)/2} \quad (549)$$

$$\text{where } \Gamma\left(\frac{x}{2}\right) = \begin{cases} (\frac{x}{2}-1)(\frac{x}{2}-2)\dots 3 \times 2 \times 1 & \text{when } x \text{ is even} \\ (\frac{x}{2}-1)(\frac{x}{2}-2)\dots 3/2 \times 1/2 \times \sqrt{\pi} & \text{when } x \text{ is odd} \end{cases}$$

v is the number of degrees of freedom of t

The Student distribution is independent of μ and σ ; its form is determined only by the number of degrees of freedom. The determination of the degrees of freedom will be described in various individual cases.

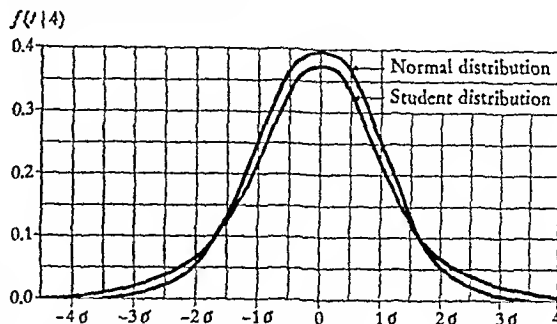


Fig. 32. Probability density of the normal distribution and of the Student distribution with degrees of freedom $v = 4$.

The Student distribution (or t -distribution) is very similar to the normal distribution and converges toward it rapidly with increasing degrees of freedom. Its range of variation is from minus infinity to infinity. It is continuous, symmetrical and bell-shaped, in contrast to the normal distribution has more probability concentrated in the tails and less in the central part.

Equations (512)–(517) for the standardized normal distribution derived from the symmetry are also valid for the Student distribution when t is replaced by t .

Tables

In the tables on pages 32–35 the exact deviations t_0 for degrees of freedom v between 1 and 200 are given for the following graphs:

$$P(\text{of the table}) = \int_{t_0}^{\infty} f(t) dt = \text{Prob}(t > t_0) \quad (a)$$

$$2P(\text{of the table}) = \int_{-t_0}^{-t_0} f(t) dt + \int_{t_0}^{\infty} f(t) dt = \text{Prob}(t < -t_0) + \text{Prob}(t > t_0) \quad (b)$$

$$\text{In one-tailed tests (confidence limits)} \alpha = P, \text{ in two-tailed tests (confidence limits)} 2\alpha = 2P. \quad (c)$$

$$\text{In accordance with (405b), the cumulative distribution } F(t) = \text{Prob}(t \leq t_0) \text{ is} \quad (d)$$

$$F(t_0) = 1 - \text{Prob}(t > t_0) = 1 - P = 1 - (551a)$$

In the table on page 42 the exact deviations t_0^* for degrees of freedom between 1 and 200 are given for the following integrals

$$P_r = \int_{t_0}^{\infty} f(t^2) dt^2 = \text{Prob}(t^2 > t_0^2) = 2\text{Prob}(t > t_0) \quad (a)$$

$$\frac{1}{2} P_r = \frac{1}{2} (552a) \quad (b)$$

$$\text{For one-tailed tests } \alpha = \frac{1}{2} P, \text{ for two-tailed tests } 2\alpha = P. \quad (c)$$

For the relationship between the Student and F -distribution (575).

12B. The χ^2 distribution

If X_1, X_2, \dots are stochastically independent observations of the same normally distributed population with mean μ and standard deviation σ , then the sum

$$\chi^2 = x_1^2 + x_2^2 + \dots + x_1^2 + \dots + x_v^2 = \sum_{i=1}^v x_i^2$$

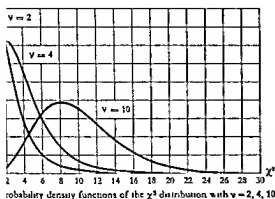
of the squares of the standardized deviations

$$x_i^2 = \left(\frac{X_i - \mu}{\sigma}\right)^2$$

has the probability density function

$$f(\chi^2|v) = \frac{1}{2^{v/2} \Gamma(v/2)} e^{-\chi^2/2} (\chi^2)^{v/2-1}; (0 \leq \chi^2 < \infty)$$

v is the number of degrees of freedom of χ^2 ; for Γ see



For $v=2$, the distribution is exponential. For $v=4$, the distribution is unimodal and skewed to the right. For $v=10$, the distribution is unimodal and more symmetric.

$$\begin{aligned} \text{Prob}(\chi^2 < x) &= \frac{1}{2^{\nu/2} \Gamma(\nu/2)} \int_0^x t^{\nu/2-1} e^{-t/2} dt \\ \text{Prob}(\chi^2 > x) &= 1 - \text{Prob}(\chi^2 < x) \end{aligned} \quad (355)$$

As $v \rightarrow \infty$, the distribution approaches a normal distribution with mean v and variance $2v$. The convergence is faster for larger v .

$$\begin{aligned} \text{Prob}(\chi^2 < x) &= \frac{1}{2^{\nu/2} \Gamma(\nu/2)} \int_0^x t^{\nu/2-1} e^{-t/2} dt \\ \text{Prob}(\chi^2 > x) &= 1 - \text{Prob}(\chi^2 < x) \end{aligned} \quad (357)$$

Calculation of the quantiles 0.005, 0.025, 0.975 and 0.995 for the confidence limits for λ of the Poisson distribution see

$$\begin{aligned} \text{Prob}(\chi^2 < x) &= \frac{1}{2^{\nu/2} \Gamma(\nu/2)} \int_0^x t^{\nu/2-1} e^{-t/2} dt \\ \text{Prob}(\chi^2 > x) &= 1 - \text{Prob}(\chi^2 < x) \end{aligned} \quad (358)$$

Tables on pages 36-39 the exact deviations χ^2 for degrees of freedom v between 1 and 200 are given for the following intervals:

$$\begin{aligned} \text{Prob}(\chi^2 < x) &= \frac{1}{2^{\nu/2} \Gamma(\nu/2)} \int_0^x t^{\nu/2-1} e^{-t/2} dt \\ \text{Prob}(\chi^2 > x) &= 1 - \text{Prob}(\chi^2 < x) \end{aligned} \quad (359)$$

Tables on pages 36-39 the exact deviations χ^2 for degrees of freedom v between 1 and 200 are given for the following intervals:

$$\begin{aligned} \frac{1}{2} \chi^2_{\alpha/2} \text{ (of the table)} &= \frac{1}{2} (558.6) \\ \text{For one-tailed } \chi^2 \text{ tests } \alpha &= \frac{1}{2} \chi^2_{\alpha} \\ \text{For two-tailed } \chi^2 \text{ tests } 2\alpha &= 1 \chi^2_{\alpha} \end{aligned} \quad (d)$$

The useful square root $\sqrt{v/\chi^2}$ for degrees of freedom between 1 and 200 is given on page 47 (confidence factors for σ) for the following quantiles

χ^2_{α}	Column 1-2 α	χ^2_{α}	Column 1-2 α
0.05 and 0.95	0.90	0.01 and 0.99	0.98
0.025 and 0.975	0.95	0.005 and 0.995	0.99

Relationships with other distributions

Normal distribution: When $v=1$, then $\chi^2_1 = t^2_{(1-p)/2}$ that is $\text{Prob}(\chi^2 < x) = 2 \text{Prob}(0 < t_r)$

F-Distribution: see (374) and (377)

Poisson distribution: The probability that a Poisson variable with mean $\chi^2/2$ takes the value x is

$$\frac{e^{-\chi^2/2} (\chi^2/2)^x}{x!}$$

This distribution is shown very clearly in Figure 44, page with $\lambda = \chi^2/2, x = \chi^2/2$.

It can be shown that if v is even

$$\text{Prob}(\chi^2 > x) = \frac{1}{2^{\nu/2} \Gamma(\nu/2)} \int_x^{\infty} t^{\nu/2-1} e^{-t/2} dt$$

For even numbers of degrees of freedom v the following quantiles can be calculated on the basis of (362) from the confidence limits for λ of the Poisson distribution, pages 107 and 108:

Prob ($\chi^2 \leq x$) = p	Argument (table on pp 107 and 108)	Page	χ^2_{α} equals
0.005	$x = v/2$	108	$2\lambda_1$
0.025	$x = v/2$	107	$2\lambda_1$
0.975	$x = (v/2) - 1$	107	$2\lambda_2$
0.995	$x = (v/2) - 1$	108	$2\lambda_2$

Example 33 [of (363)] Required: Solution

$$\begin{aligned} \chi^2_{0.005, 153} &= 130.8, \chi^2_{0.025, 153} = 108.61, \chi^2_{0.975, 153} = 129.56, \chi^2_{0.995, 153} = 153.30 \end{aligned}$$

The value $\lambda_r = 153.30$ has been interpolated linearly:

$$154.39 - \lambda_r (154.39 - 143.52) = 153.30$$

$$\lambda_{153} = 1/10 (\lambda_{154} - \lambda_{143}) \sim \lambda_{153}$$

The addition theorem for the χ^2 distribution

In equation (363) the sum can be broken up into any number parts, for example

$$x^2 = \frac{x_1^2 + x_2^2}{x^2(v-2)} + \frac{x_3^2 + x_4^2 + x_5^2 + x_6^2}{x^2(v-4)} + \frac{x_7^2 + \dots}{x^2(v-\dots)} \text{ etc}$$

It follows that

If $x_1^2, x_2^2, \dots, x_n^2$ are stochastically independent and the χ^2 distributions have the degrees of freedom v_1, v_2, \dots, v_n respectively, then the sum $x^2 = x_1^2 + x_2^2 + \dots + x_n^2$ likewise has a χ^2 distribution with $v = v_1 + v_2 + \dots + v_n$ degrees of freedom

$$x^2 = x_1^2 + x_2^2 + \dots + x_n^2 \quad (36)$$

There is also a division theorem for χ^2 on which the analysis of regression and variance is based. For further details the reader is referred to the literature.

χ^2 and sample variance

In accordance with (553), $\chi^2 \sim [\Sigma(x - \mu)^2]/\sigma^2$. If μ is replaced by \bar{x} , then from (493c), $\Sigma(x - \bar{x})^2 \sim (N - 1)s^2$. If now $N - 1$ is replaced by ν , then νs^2 is eventually obtained in place of $\Sigma(x - \mu)^2$. Intuitively it is surmised that

$$\chi^2 \sim \frac{\nu s^2}{\sigma^2}, \text{ where } \nu = \text{degrees of freedom of } s^2 \quad (565)$$

and this is a good guess. It should be noted that (565) is a second definition of χ^2 equivalent to (553) but valid only for normally distributed populations.

An important asymptotic property of χ^2

Given is a sample divided into n classes from a population of any form. If f_i is the observed frequency of the class i , where $f_1 + f_2 + \dots + f_n = N$, then f_i is known as the empirical (absolute) frequency. If p_i is the given or a hypothetical probability that the variable x will fall in the class i , where $p_1 + p_2 + \dots + p_n = 1$, then Np_i is known as the given or the hypothetical (absolute) frequency. The empirical frequencies in the individual classes are random variables. In this case

$$\sum_{i=1}^n \frac{(f_i - Np_i)^2}{Np_i} \rightarrow \chi^2; \text{ where } \nu = n - 1 \quad (566)$$

when $\nu \rightarrow \infty$.

(566) was discovered by K. PEARSON. The fact that it is exactly valid only when $\nu \rightarrow \infty$ is of little consequence in practice but gives rise to certain restrictions:

In tests for goodness of fit based on (566), the samples as a whole should not be too small, the hypothetical (absolute) frequencies in the individual classes not below $Np_i = 4$. If they are less than this, they should be increased to the required level by combining 2, 3, ... neighbouring classes. This is necessary, however, only when the number of classes is small. If ν is greater than (about) 8 and the sample size over 40, then it is permissible for Np_i in isolated classes to be as low as 1.

As a rule the hypothetical frequencies are not given:

Theoretical (absolute) frequencies Np_i which have been calculated on the basis of estimated parameters are known as fitted frequencies; the theoretical distribution corresponding to them is known as the fitted distribution. (568)

If k parameters must be estimated in the calculation of fitted frequencies, then the number of degrees of freedom for χ^2 defined by (566) is $\nu = n - 1 - k$, where n = number of classes. (a)

m samples each grouped into n classes (in an $m \times n$ contingency table) are submitted to a χ^2 test based on (566), then the number of degrees of freedom for χ^2 is $\nu = (n - 1)(m - 1)$. (b) (569)

In the special case, frequently encountered, of the 2×2 table, $\nu = 1$. (c)

For an example of a χ^2 test with estimation of parameters see section 11F (b), page 164. Another χ^2 test is described in section 23, page 191, in which further tests for frequency are dealt with. In conclusion it should be noted that definitions (553) and (565) differ fundamentally from definition (566) in spite of the fact that the formulae are very similar: (553) and (565) are valid only for normally distributed populations, (566) is valid for populations of any form; (553) and (565), \bar{x} and s are continuous variables, while in (566), f_i is a discrete variable.

When χ^2 tests are carried out with the aid of fitted distributions, it must be taken that the estimates made satisfy condition (430) (431).

C. The F -distribution (variance-ratio distribution)

In the expression F -distribution, the letter F symbolizes not a cumulative distribution but the name of R.A. FISHER, the discoverer of the z -distribution, which is equivalent to the F -distribution¹⁴.

If s_1^2 and s_2^2 are two stochastically independent estimate variance σ^2 of the same normally distributed population, then in accordance with (565)

$$s_1^2 = \sigma^2 \frac{\chi_1^2}{\nu_1} \text{ and } s_2^2 = \sigma^2 \frac{\chi_2^2}{\nu_2}$$

It follows that the quotient

$$F = \frac{s_1^2}{s_2^2} = \frac{\chi_1^2/\nu_1}{\chi_2^2/\nu_2}; 0 \leq F < \infty$$

(ν_1 and ν_2 are the degrees of freedom of s_1 and s_2 respectively)

has the probability density function

$$f(F) = \frac{\Gamma\left(\frac{\nu_1 + \nu_2}{2}\right)}{\Gamma\left(\frac{\nu_1}{2}\right) \Gamma\left(\frac{\nu_2}{2}\right)} \frac{\nu_1^{\nu_1/2} \nu_2^{\nu_2/2}}{(F\nu_1 + \nu_2)^{(\nu_1 + \nu_2)/2}} F^{\nu_1/2 - 1}; 0 \leq F < \infty$$

[for Γ see (549)]

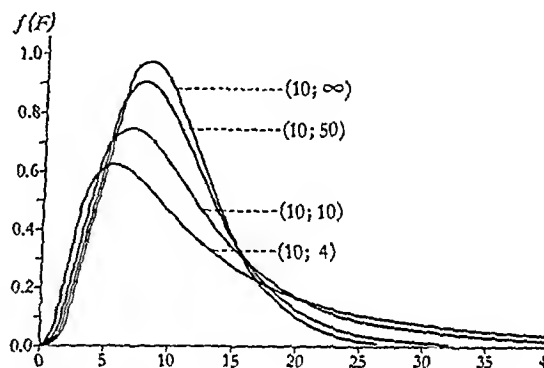


Fig. 34. Probability density functions of the F -distribution with various degrees of freedom (ν_1, ν_2).

The F -distribution is a continuous unimodal distribution with a range of variation from zero to infinity.

Parameters

$$\begin{aligned} \text{Mean } \mu &= \nu_2/(\nu_2 - 2); \nu_2 > 2 & (a) \\ \text{Variance } \sigma^2 &= \left(\frac{\nu_2}{\nu_2 - 2}\right)^2 \times \frac{2(\nu_1 + \nu_2 - 2)}{\nu_1(\nu_2 - 4)}; \nu_2 > 4 & (b) \end{aligned} \quad (57)$$

Interchange of ν_1 and ν_2

$$F_0(p; \nu_1; \nu_2) = 1/[F_0(1 - p; \nu_2; \nu_1)] \quad (58)$$

In (573), p can be $\text{Prob}(F > F_0)$ just as well as $\text{Prob}(F < F_0)$.

Tables

The values of F_0 given on pages 40 and 41 satisfy the following equation:

$$\begin{aligned} P(\text{of the table}) &= P_r = \int_{F_0}^{\infty} f(F) dF = \text{Prob}(F > F_0) & (a) \\ \text{In one-tailed tests } \alpha &= P, \text{ in two-tailed tests } 2\alpha = 2P & (b) \\ \text{On the } t^2 \text{ table of page 42 see } & (575) \text{ and } (552). & (c) \end{aligned} \quad (57)$$

Relationships to other distributions

Student distribution:

$$\begin{aligned} \text{Prob}[(F > F_0) | 1; \nu_2] &= \text{Prob}(t^2 > t_0^2 | \nu_2) \\ &= 2 \text{Prob}(t > t_0 | \nu_2) \end{aligned} \quad (57)$$

For $F(1; \nu_2)$ with ν_2 values between 1 and 200, the more comprehensive t^2 table on page 42 should therefore be used. For explanation see (552).

χ^2 distribution:

When F_p and χ_p^2 denote quantiles

$$F_p(v_1; \infty) = \frac{x_{p, v_1}^2}{v_1} \quad (a)$$

$$F_p(\infty; v_2) = \frac{v_2}{x_{1-p, v_2}^2} \quad (b)$$

From (376) and (356a) it follows that

$$\left. \begin{aligned} F(v_1; \infty) &\rightarrow 1, \text{ when } v_1 \rightarrow \infty \\ F(\infty; v_2) &\rightarrow 1, \text{ when } v_2 \rightarrow \infty \end{aligned} \right\} \text{ that is, } F(\infty; \infty) = 1 \quad (377)$$

Binomial distribution:

$$\left. \begin{aligned} \text{Prob} \left\{ F(v_1; v_2) < \frac{N-x}{x+1} \times \frac{p}{1-p} \right\} \\ = \sum_{x=0}^N \binom{N}{x} p^x (1-p)^{N-x} \\ \text{where } N = \frac{v_1 + v_2}{2} - 1 \\ x = \frac{v_1}{2} - 1 \end{aligned} \right\} \quad (378) \quad \left. \begin{aligned} v_1 \text{ and } v_2 \text{ are even numbers} \end{aligned} \right\}$$

On the basis of (378) the following quantiles F_p can be calculated from the confidence limits for p of the binomial distribution (pages 85-98)

Prob ($F < F_p$)	Arguments (pages 85-98)			Quantile F_p
	Col- umn	N	x	
0.005	99%	$\frac{v_1 + v_2}{2} - 1$	$\frac{v_1}{2} - 1$	$\frac{p_1}{p_2}$
0.025	95%			$\frac{p_1}{p_2}$
0.975	95%			$\frac{p_1}{p_2}$
0.995	99%			$\frac{p_1}{p_2}$

Example 14 $F_{0.995}$ (152, 36) is required. We have $N = 93$, $x = 75$, $p_1 = 0.8993$ (from page 96), $p_2(1-p) = 8.93049$, $v_1/v_2 = 0.236842$, $F_{0.995}$ (152, 36) = 2.12.

12. The normally distributed population: Confidence and tolerance intervals

(Cf. also section 8, page 154)

12A Confidence intervals for the mean μ

One-sided confidence interval with *singles upper limit*

$$\left. \begin{aligned} \text{Prob} (-\infty < \mu < \bar{x} + k \times S_d) = 1 - \alpha \\ \text{[cf. also (380J)]} \end{aligned} \right\} \quad (a)$$

One-sided confidence interval with *singles lower limit*

$$\left. \begin{aligned} \text{Prob} (\bar{x} - k \times S_d < \mu < \infty) = 1 - \alpha \\ \text{[cf. also (380J)]} \end{aligned} \right\} \quad (b)$$

Two-sided confidence interval with *symmetrical limits*

$$\left. \begin{aligned} \text{Prob} (\bar{x} - k \times S_d < \mu < \bar{x} + k \times S_d) = 1 - 2\alpha \\ \text{[cf. also (380J)]} \end{aligned} \right\} \quad (c)$$

Factors $k \times S_d$ for (380a, b, c)				
Equations	Degrees of freedom v of t	k	S_d	Page (r, t or k)
(a) and (b)	> 200	$t_{\alpha/2} / \sqrt{N}$	σ or t	28
(a) and (b)	≤ 200	$t_{\alpha/2} / \sqrt{N}$	$t_{\alpha/2}$	32-35
(c)	> 200	$k_{\alpha/2} \text{ or } t_{\alpha/2} / \sqrt{N}$	σ or t	k_2 43, t 28
(c)	≤ 200	$k_{\alpha/2} \text{ or } t_{\alpha/2} / \sqrt{N}$	$t_{\alpha/2}$	k_2 43, t 32-35

In the table on page 43 (for k_2) the number of degrees of freedom $v = N - 1$ is contained in the argument N . In this table the transition from t to s takes place at $N = 201$.

12B. Tolerance intervals

Tolerance intervals without confidence probability

One-sided tolerance interval with *singles upper limit*

$$\left. \begin{aligned} \text{Prob} (-\infty < x < m + k \times S_d) = 1 - \alpha = \beta_p; \\ \text{[cf. also (381d)]} \end{aligned} \right\} \quad (a)$$

One-sided tolerance interval with *singles lower limit*

$$\left. \begin{aligned} \text{Prob} (m - k \times S_d < x < \infty) = 1 - \alpha = \beta_p; \\ \text{[cf. also (381d)]} \end{aligned} \right\} \quad (b)$$

Two-sided tolerance interval with *symmetrical limits*

$$\left. \begin{aligned} \text{Prob} (m - k \times S_d < x < m + k \times S_d) = 1 - 2\alpha = \beta_p \\ \text{[cf. also (381d)]} \end{aligned} \right\} \quad (c)$$

m, k and S_d for (381a, b, c)						
Equations	Degrees of freedom v of t	Known parameters or estimates	m	k	S_d	Page (r, t, k)
(a) and (b)	> 200	μ, σ or \bar{x}, s	μ or \bar{x}	k_{α}	σ or s	28
(a) and (b)	≤ 100	μ, σ	μ	k_{α}^*	σ	44, col 1
(a) and (b)	≤ 100	μ, s	μ	k_{α}	s	32-35
(a) and (b)	≤ 100	μ, s	\bar{x}	k_{α}^*	s	44, col 2
(c)	> 200	μ, σ or \bar{x}, s	μ or \bar{x}	k_{α}	σ or s	28
(c)	≤ 100	μ, σ	μ	k_{α}	σ	44, col 1
(c)	≤ 100	μ, s	μ	k_{α}	s	32-35
(c)	≤ 100	μ, s	\bar{x}	k_{α}	s	44, col 2

* β_p in the table is selected as follows: β_p (required) = $1 - 2\alpha$, α is given

Tolerance intervals with confidence probability β_1

Equations (381a, b, c) are applicable with the following complementary equation [example of (381d)]

$$\text{Prob} [\text{Prob} (m - k \times S_d < x < m + k \times S_d) \geq 1 - 2\alpha] = \beta_1$$

m, k and S_d for (381a, b, c)						
Equations	Degrees of freedom v of t	Known parameters or estimates	m	k	S_d	Page (r, t, k)
(a) and (b)	≤ 100	μ, σ	μ	k_{α}^*	σ	44, col 3
(a) and (b)	≤ 100	μ, s	μ	k_{α}^*	s	44, col 4
(a) and (b)	≤ 1000	μ, s	\bar{x}	k_{α}	s	45-46
(c)	≤ 100	μ, σ	μ	k_{α}	σ	44, col 3
(c)	≤ 100	μ, s	μ	k_{α}	s	44, col 4
(c)	≤ 1000	μ, s	\bar{x}	k_{α}	s	45-46

* β_p in the table is selected as follows: $\beta_p = 1 - 2\alpha$, α is given

The following equations are valid for the confidence and tolerance factors

$$\left. \begin{aligned} k_{\alpha} &= t_{\alpha, N-1} \times 1/\sqrt{N} \text{ for } N \leq 201 \\ &= |t_{\alpha}| \times 1/\sqrt{N} \text{ for } N > 201 \\ k_{\alpha} &= |t_{\alpha}| \times \sqrt{1 + 1/N} \\ k_{\alpha} &= t_{\alpha, N-1} \times \sqrt{1 + 1/N} \\ k_{\alpha} &= \text{solution of } \int f(t) dt = \beta_p, (t' = t_{\alpha}) \\ k_{\alpha} &= |t_{\alpha}| \times \sqrt{(N-1)/\chi_{1-\beta_1, N-1}^2} \\ k_{\alpha} &\text{ cf. EISENHART et al., pages 108-109} \end{aligned} \right\} \quad (382)$$

12C. Confidence intervals for the standard deviation σ

From (382), it follows that:

$$\left. \begin{aligned} \text{Prob} (k_2 s_{\alpha} < \sigma < k_1 s_{\alpha}) = 1 - 2\alpha \\ \text{where } k_2 = \sqrt{v/\chi_{1-\alpha}^2} \text{ and } k_1 = \sqrt{v/\chi_{\alpha}^2} \end{aligned} \right\} \quad (384)$$

Values of k_1 and k_2 for degrees of freedom between 1 and 100 are given in the left-hand table on page 47.

14. The normally distributed population: Extreme range and extreme deviations

14A. The extreme range

Definition

If x_1 is the lowest and x_n the highest value of a sample of size n , then $(x_n - x_1)$ is the extreme range w_n of this sample. (585)

The standardized extreme range of a sample of size n from a population with standard deviation σ is

$$W_n = \frac{w_n}{\sigma} = \frac{x_n - x_1}{\sigma} \quad (586)$$

The mean extreme range of m samples of size n from one and the same population is

$$\bar{w}_{m,n} = \frac{\sum_1^m w_n}{m} = \frac{\sum_1^m (x_n - x_1)}{m} \quad (587)$$

and the standardized mean extreme range is

$$\bar{W}_{m,n} = \frac{\bar{w}_{m,n}}{\sigma} = \frac{\sum_1^m w_n}{m\sigma} = \frac{\sum_1^m (x_n - x_1)}{m\sigma} \quad (588)$$

Since the extreme range w_n is merely a special case of the mean extreme range $\bar{w}_{m,n}$ with $m = 1$, only the mean extreme range will be referred to in the text that follows.

Mean extreme range as a multiple of σ

The expected value \bar{W}_n of the extreme range of random samples of size n from a normally distributed population with unit standard deviation satisfies the relation

$$\bar{W}_{m,n} \rightarrow \bar{W}_n \quad (589)$$

The upper right-hand table on page 47 gives values of \bar{W}_n for the standardized normal distribution as multiples of σ^{16} . (Many authors use the symbol d_n in place of \bar{W}_n .)

σ as a fraction of the mean extreme range

The quotient

$$\frac{\bar{w}_{m,n}}{\bar{W}_n} = \bar{w}_{m,n} \times A_n \quad (590)$$

gives an unbiased estimate of σ . Values of this quotient are given in the lower right-hand table on page 47.

The relative efficiency of (590) compared with that of the estimate $[s^2 \text{ from (492a)}]$ when $m = 1$ is¹⁷

n	2	3	4	5	6	10	15	20	50	100	∞
Efficiency	1.00	0.99	0.98	0.96	0.93	0.85	0.77	0.70	0.49	0.34	0

For sample sizes between 2 and 10 there is thus little difference between the two estimates. Within this range (590) is useful as a *aid method of estimating σ* but it should not be used in place of s in a standard *t* test.

For larger samples the extreme range of σ can likewise be accurately estimated, namely by dividing the sample into a number of independent subgroups of the same size between 2 and 10 and taking their extreme ranges. In accordance with (588), the mean of these ranges is then the mean extreme range. However, a subdivision must be effected by a *random selection* among the whole sample values. If there is no natural method of doing this (such as using the order in time of obtaining the sample values), random numbers may be used, but the time needed to carry out the subdivision will tend to nullify the advantages of the more rapid calculation.

Overlapping groups must of course be avoided, since these would obviously be dependent.

σ as a fraction of the mean extreme range

The quotient

$$\frac{\bar{w}_{m,n}}{\bar{W}_n \sqrt{m}} = \bar{w}_{m,n} \times A_{m,n}$$

where $m =$ sample size N , gives an unbiased estimate of standard deviation σ of the estimate \bar{x} . Values of the $A_{m,n}$

$$A_{m,n} = 1/(\bar{W}_n \times \sqrt{m})$$

are given in the table on page 48.

Example 36 (section 14A). Given is the sample 3.1, 2.08, 2.10, 2.67. The estimates of σ and $\sigma_{\bar{x}}$ on the basis of the extreme range or mean extreme range are

(a) 1 extreme range

$$1.34 - 3.00: \text{ range} = 1.66 \quad \sigma' = 1.66 \times 0.231 = 0.383$$

(b) 2 extreme ranges

$$\left. \begin{array}{l} 1.34 - 3.00 \\ 2.08 - 2.67 \end{array} \right\} \text{ mean} = 1.125 \quad \sigma' = 1.125 \times 0.59 = 0.664$$

(c) 3 extreme ranges

$$\left. \begin{array}{l} 1.56 - 3.00 \\ 1.34 - 2.08 \\ 2.10 - 2.67 \end{array} \right\} \text{ mean} = 0.916 \quad \sigma' = 0.916 \times 0.88 = 0.806$$

For comparison, σ can be estimated using (492b) with $s = 0.63257$. In order to correct the bias of this estimate, s must be multiplied by the factor $k_s = 1.0509$ (see the left-hand table on page 47, column k_s), giving the result $s = 0.665$ and $\sigma_{\bar{x}} = 0.208$.

All the above estimates may be regarded as equally good, though the agreement between s and the estimates (a) and (c) is striking, this does not mean that estimate (c) is not a further sample from the same population could result in a value nearer to (c).

14B. Testing extreme ranges and extreme deviations

The 'studentized' extreme range (table on page 51, sample size N)

In the test quotients

$$\frac{x_N - x_1}{s_v}$$

($v =$ degrees of freedom of s ; $x_1 < x_2 < \dots < x_N$)

s is an estimate calculated from a sample *different* from that of the sample to be tested but originating from the same population. If the test quotient attains or exceeds the level in the table corresponding to the degrees of freedom v , and the sample size N , then the extreme range in question is *too large* (significance probability α).

If σ is known, the levels at $v = \infty$ should be used. If the sample size exceeds the range of the table, testing should be carried out according to (596d) for sample sizes between 21 and 25 and according to (595) for still larger samples, if it is desired to test extreme ranges.

The 'studentized' extreme deviation (table on page 52, sample size N)

In the test quotients

$$\frac{x_N - \bar{x}}{s_v} \text{ or } \frac{\bar{x} - x_1}{s_v}$$

($v =$ degrees of freedom of s ; $x_1 < x_2 < \dots < x_N$)

s has the same meaning as in (592). If σ is known, the levels at $v = \infty$ should be used. If the test quotient attains or exceeds the level in the table corresponding to the degrees of freedom v and the sample size N , then the extreme deviation in question is *too large* (significance probability α).

If the sample size exceeds the range of the table, testing should be carried out according to (596c and d) for sample sizes between 10 and 25 and according to (595) for still larger samples.

standardized extreme deviation (upper table on page 52)

We have

$$\text{Prob} (x \leq e_1) = \left[\int_{-\infty}^{e_1} f(x) dx \right]^N, \text{ for } e_1 \text{ sec (595)} \quad (a) \quad (594)^*$$

$$\text{Prob} (-e_2 \leq x \leq e_2) = \left[\int_{-e_2}^{e_2} f(x) dx \right]^N \quad (b) \quad (594)^*$$

e_1, e_2 = standardized extreme deviation; N = sample size

In the test quotients

$$\frac{x_N - \mu}{\sigma} \text{ or } \frac{\mu - x_1}{\sigma} = e_1 \quad (595)$$

e symbols have the customary meaning. For sample sizes over 25, μ and σ can be replaced by \bar{x} and s for smaller samples (593) could be used.

using extreme values of a sample on the basis of their own attributes** (upper left-hand table on page 53, sample size 3-25)

When no independent information on the standard deviation of the population is available, extreme deviations in samples up to a size of 25 can be tested by means of the following quotients*

Sample size N	Quotient	Sample size N	Quotient
3-7	$\frac{x_N - x_{N-1}}{x_N - x_1} \quad (a)$	11-13	$\frac{x_N - x_{N-1}}{x_N - x_1} \quad (c)$
8-10	$\frac{x_N - x_{N-1}}{x_N - x_2} \quad (b)$	14-25	$\frac{x_N - x_{N-1}}{x_N - x_2} \quad (d)$

where $\left\{ \begin{array}{l} x_1 < x_2 < \dots < x_N, \text{ when a right-hand extreme value is tested,} \\ x_N < x_{N-1} < \dots < x_1, \text{ when a left-hand extreme value is tested} \end{array} \right.$

With samples of over 25, (595) should be used with μ and σ replaced by \bar{x} and s

General considerations in testing extreme values

It is common for extreme values to be ignored, often without comment by the author and without their first being tested statistically. Occasionally they are even eliminated before the experimental data are put into the hands of the statistician. This is clearly undesirable, for in some situations extreme values are often the most

reveals a causal circumstance accounting for its existence. Examples would be an error made in measurement or calculations, the un-

to contain extreme values of the population. A small sample containing an extreme value can give a completely false picture of the population it represents. In such cases the extreme value may be removed. However, it is advisable to use a small significance prob-

peculiarly dependent on this condition of normality

* This formula is derived from (387) and (495 a) or (497 c)

Special considerations in testing extreme values

If testing in accordance with (592) results in the postulated signifi-

It is permissible to test extreme values more than once in the same sample. In this case the sample size must be reduced by one after each rejection before a new test is made. The resulting level of significance α_{res} for the total number k of significant tests then has the very approximate order of magnitude

$$\alpha_{res} \sim 1 - (1 - \alpha_1)(1 - \alpha_2) \dots (1 - \alpha_k)$$

Example 37. The sample of example 24, page 160, is to be tested using (594 d).

1st test ($N = 21$)

$$\text{Right-hand extreme deviate } \frac{4.41 - 2.68}{4.41 - 1.76} = 0.653, \text{ deviate is too large } (\alpha < 0.005)$$

2nd test ($N = 20$)

$$\text{Right-hand extreme deviate } \frac{3.56 - 2.35}{3.56 - 1.76} = 0.672; \text{ deviate is too large } (\alpha < 0.005)$$

Only the 5th test gives no further significant deviation

After two deletions $\alpha_{res} \sim 1 - (> 0.995) (> 0.995) < 0.01$, if the sample were from a normally distributed population. This is not the case (cf section 10 H, page 161), so that the extreme values may on no account be rejected

15. The normally distributed population: Comparison of a sample with the hypothetical population

15A. Comparison of the sample and population standard deviations s and σ (or of the variances s^2 and σ^2)

The confidence limits for σ are obtained from (584), those for σ^2 analogously by replacing s by s^2 and k by k^2 . The hypothetical σ or σ^2 is then compared with these limits and the result interpreted in accordance with (474)

15B. Comparison of the sample and population means \bar{x} and μ

Comparison of the estimate \bar{x} with the hypothetical mean is made by means of the test quotients given in (598)-(602), the numerical value of the quotient being compared with the limit given*

If the test quotient is smaller than the limit, then the result is interpreted in accordance with (474) or (475). If it attains or exceeds the limit, then

	Significance in brackets	
	One tailed test	Two tailed test
When $\bar{x} - \mu < 0$	$\bar{x} < \mu (\alpha)$	$\bar{x} \neq \mu (2\alpha)$
When $\bar{x} - \mu > 0$	$\bar{x} > \mu (\alpha)$	

The t -test (normal distribution)

Applicability When σ is known or when the degrees of freedom of $s = N - 1 > 200$

Test quotient	Significance limit
$\left \frac{\bar{x} - \mu}{\sigma} \sqrt{N} \right $ or $\left \frac{\bar{x} - \mu}{s_{N-1}} \sqrt{N} > 201 \right $	$ z_\alpha $, page 28 (a)
$\frac{(\bar{x} - \mu)^2 N}{\sigma^2}$ or $\frac{(\bar{x} - \mu)^2 N}{s_{N-1}^2} > 201$	$\chi_{2, \alpha}^2$, page 36, $\alpha = \frac{1}{2} \alpha$, $2\alpha = 1\%$ (b)
$\left \frac{\bar{x} - \mu}{s_{N-1}} \right : N > 201$	t/\sqrt{N} = confidence factor k_α , page 43 (c)

The *t*-test (Student distribution)

Applicability: When σ is unknown and the degrees of freedom of $s = N - 1 \leq 200$

Test quotient	Significance limit	
$\frac{ s - \mu }{s_{N-1}}; N \leq 201$	t_{N-1} , pages 32-35; $\alpha = P, 2\alpha = 2P$	(a)
$\frac{(s - \mu)^2 N}{s_{N-1}^2}; N \leq 201$	t_{N-1}^2 , page 42; $\alpha = \frac{1}{2}P, 2\alpha = P$; cf. (552)	(b)
$\frac{ s - \mu }{s_{N-1}}; N \leq 201$	$t_{N-1}/\sqrt{N} = \text{confidence factor } k_2$, page 43	(c)

(599)

LORD's test based on the extreme range¹⁹

Applicability: Samples of size $N \leq 20$ (a) and $N > 20$ (b)

Test quotient	Significance limit	
$\frac{ s - \mu }{s_{N-1}}; N \leq 20;$ $x_1 < x_2 < \dots < x_N$	Page 53, middle left-hand table	(a)
$\frac{ s - \mu m}{[\sum (x_n - x_1)] A_{m,n}};$ $m \times n = N$	Page 49; $A_{m,n}$ page 48	(b)

(600)

m = number of subgroups of size n (cf. section 14 A, page 170) in which $x_1 < x_2 < \dots < x_n$

The midrange test based on the extreme range²⁰

Applicability: Samples of size $N \leq 10$

Test quotient	Significance limit	
$\frac{ x_N + x_1 - 2\mu }{x_N - x_1}; N \leq 10$	Page 53, upper right-hand table	(601)

WALSH test^{20, 21}

Applicability: Samples of size $4 \leq N \leq 14$ from any symmetrical population

Test quotient	Significance limit	
Page 53, lower right-hand table	Page 53, lower right-hand table	(602)

Note that while the use of (598b) and (599b) involves the squaring of $(s - \mu)$ it obviates extracting the square root of s^2 (provided s is not required). The use of (598c) and (599c) avoids the multiplication by \sqrt{N} , with the further advantage that the transition from t to r in using the table on page 43 is quite 'automatic'.

(600)–(602) are straightforward rapid tests [especially (601)] in which even \bar{x} does not need to be calculated. Within the tabulated range their power is practically the same as that of (599). The WALSH test is suitable not only for normal but also for any other symmetrical distribution. In this case, the significance probability for N up to 8 is somewhat higher than that in the table. For $N > 8$ the values in the table are exact.

When a calculating machine is not available, multiplication is faster than division. In this event, the significance limit should be multiplied by the divisor of the test quotient in order to obtain the limit for the dividend.

Example 38. When t is the limit for $\frac{|x - \mu|}{s_{N-1}}$, then $t s$ is the limit for $|x - \mu|$.

16. The normally distributed population: Comparison of two samples

In comparing two samples, the following hypotheses concerning the parameters of the original populations must be taken into consideration:

$$\begin{aligned} \sigma_1^2 = \sigma_2^2 & \left\{ \begin{array}{l} \mu_1 = \mu_2 \\ \mu_1 \neq \mu_2 \end{array} \right. & \begin{array}{l} (a) \\ (b) \end{array} & (603) \\ \sigma_1^2 \neq \sigma_2^2 & \left\{ \begin{array}{l} \mu_1 = \mu_2 \\ \mu_1 \neq \mu_2 \end{array} \right. & \begin{array}{l} (a) \\ (b) \end{array} & (604) \end{aligned}$$

16A. Comparison of variances

The test quotient for the hypothesis ($\sigma_1^2 = \sigma_2^2$) (603) is (570), in which the larger of the two sample variances must always be made the numerator. This means that renumbering of the variances with respect to the indices of the table is necessary when s_1^2 (from sample 1) is smaller than s_2^2 . The number of degrees of freedom v_1 in the tables on pages 40 and 41 is always that of the numerator of (570).

s_1^2 and s_2^2 must be calculated from (492). Their degrees of freedom are $v_1 = N_1 - 1$ and $v_2 = N_2 - 1$.

If the test quotient is smaller than the significance limit F in the table on pages 40 and 41, then in accordance with (474) it can be assumed that $\sigma_1^2 = \sigma_2^2$. In this case the means are tested by the procedure given in section 16B below. If the test quotient attains or exceeds the significance limit F , then $\sigma_1^2 > \sigma_2^2$ (significance probability $\alpha = P$) or $\sigma_1^2 \neq \sigma_2^2$ (significance probability $2\alpha = 2P$). The means are tested by the procedure given in section 16C, page 17.

16B. Comparison of means when $\sigma_1^2 = \sigma_2^2$

The following symbols are used here:

$$|\bar{x}_1 - \bar{x}_2| = d \text{ and } |\mu_1 - \mu_2| = d \quad (606)$$

The estimate of the common standard deviation $\sigma = \sigma_1 = \sigma_2$ is

$$s = \sqrt{\frac{S_1 + S_2}{N_1 + N_2 - 2}}; S_1 \text{ and } S_2 \text{ from (493)} \quad (607)$$

$$v_s = v_1 + v_2 = N_1 + N_2 - 2$$

The estimate of the standard deviation of the difference d is

$$s_d = s \sqrt{\frac{1}{N_1} + \frac{1}{N_2}}; s \text{ from (607); } v_{s_d} = N_1 + N_2 - 2 \quad (608)$$

If σ is known, s is replaced by σ in (608). If $N_1 = 1$, then $s_d = s/\sqrt{1 + 1/N_2}$, $v = N_2 - 1$; cf. also (452) and (583c and e).

The test quotients for the hypotheses ($\mu_1 = \mu_2$ | $\sigma_1^2 = \sigma_2^2$) are

$$\begin{aligned} & \text{if } \sigma \text{ is known or } v > 200 \\ & d/s_d \text{ or } d/s_d; \text{ limit } |t_\alpha|, \text{ page 28} & (a) \\ & \text{when } v \leq 200 \\ & d/s_d; \text{ limit } t_\alpha, \text{ pages 32-35; } \alpha = P, 2\alpha = 2P & (b) \\ & \text{or} \\ & d^2/s_d^2; \text{ limit } t_\alpha^2 [= F(1; v)], \text{ page 42; } \alpha = \frac{1}{2}P, 2\alpha = P & (c) \end{aligned} \quad (609)$$

If the test quotient attains or exceeds the significance limit, then this is considered as evidence that $\mu_1 \neq \mu_2$. In this case it is often desirable to test the hypothesis ($\mu_1 - \mu_2 = d$ | $\sigma_1^2 = \sigma_2^2$):

The test quotients are obtained by replacing d in (609) by $|d - d|$. If the quotient exceeds the significance limit, then this is considered as evidence that $\mu_1 - \mu_2 \neq d$. (610)

The confidence limits for d are

$$\begin{aligned} & \text{two-sided} \\ & \text{Prob}(d - t_{v_s} \times s_d \leq d \leq d + t_{v_s} \times s_d) = 1 - 2\alpha & (a) \\ & \text{one-sided with a single upper limit} \\ & \text{Prob}(d \leq d + t_{v_s} \times s_d) = 1 - \alpha & (b) \end{aligned} \quad (611)$$

If the test quotient in (609) is smaller than the significance limit, then it may be assumed in accordance with (474) that $\mu_1 = \mu_2$. Since also $\sigma_1^2 = \sigma_2^2$, the conclusion may be drawn that the two samples 1 and 2 originated from the same population with mean μ and variance σ^2 . Estimates of these parameters are

$$\bar{x} = \frac{\sum_{i=1}^{N_1} x_1 + \sum_{i=1}^{N_2} x_2}{N_1 + N_2} = \frac{N_1 \bar{x}_1 + N_2 \bar{x}_2}{N_1 + N_2} \quad (612)$$

$$s^2 = \frac{S_1 + S_2 + \frac{(\sum_{i=1}^{N_1} x_1)^2}{N_1} + \frac{(\sum_{i=1}^{N_2} x_2)^2}{N_2} - \frac{(\sum_{i=1}^{N_1} x_1 + \sum_{i=1}^{N_2} x_2)^2}{N_1 + N_2}}{N_1 + N_2 - 1} \quad (613)$$

where $v_s = N_1 + N_2 - 1$; S_1 and S_2 from (493).

16C. Comparison of means when $\sigma_1^2 \neq \sigma_2^2$

If σ_1 and σ_2 are known, or $N_1 + N_2 > 200$, then

$$\sigma_d = \sqrt{\frac{\sigma_1^2}{N_1} + \frac{\sigma_2^2}{N_2}} \quad \text{and} \quad s_d = \sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}} \quad (614)$$

and the test quotients

$$\frac{d}{\sigma_d} \quad \text{and} \quad \frac{d}{s_d} \quad \text{or} \quad \frac{|d - \ell|}{\sigma_d} \quad \text{and} \quad \frac{|d - \ell|}{s_d} \quad (615)$$

have the same limits as (609a)

If σ_1 and σ_2 are unknown, then the test quotients

$$\frac{d}{\sigma_d} \quad \text{and} \quad \frac{|d - \ell|}{s_d} \quad (616)$$

have the same limits as (609b)²³, where

$$\left. \begin{aligned} s_d &= \sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}} & (a) \\ v &= \frac{1}{k^2/v_1 + (1-k)^2/v_2} & (b) \\ k &= \frac{N_1 s_1^2}{N_1 s_1^2 + N_2 s_2^2} & (c) \end{aligned} \right\} \quad (617)$$

(v_1 and v_2 are degrees of freedom of s_1 and s_2 respectively)

16D. Testing pair differences

When two analytical methods can be tried out on the same substrate, or two methods of treatment on the same individual, then the *pair* of a test is considerably greater in place of the difference between two means, one mean calculated from the sum of the pair differences is tested.

Let A and B be the methods to be compared, $A_i - B_i = d_i$ the difference between the two methods for the i th individual.

16D because of the non-independent nature of the samples

16E. Tests for two samples using the extreme range²⁴

(a) Two samples of the same size $N' = N'' = N \leq 20$

$x'_m = x'_1$ and $x''_m = x''_1$ are the extreme ranges of these samples, the test quotient is then

$$\frac{|R' - R''|}{x'_m - x'_1 + x''_m - x''_1} \quad (618)$$

(for limit see page 53, bottom left-hand table)

(b) Two samples of unequal size, or of the same size but larger than in (a)

The samples are divided respectively into m' and m'' random subgroups of the same size n (cf. section 14A, page 170). The sum of all the extreme ranges of these subgroups from both samples is denoted by S_x . The test quotient is then

$$\frac{S_x - \bar{x}^2 / \sqrt{m' m''}}{S_x \times A_{m, n}} \quad (\text{for } A_{m, n} \text{ see page 49}) \quad (619)$$

17. The normally distributed population: Testing several samples

Given are n samples of sizes

$$N_1, N_2, \dots, N_n, \text{ where } \sum_{i=1}^n N_i = N \quad (a)$$

The sums of the individual values x are

$$\sum_{i=1}^n x_{i1}, \sum_{i=1}^n x_{i2}, \dots, \sum_{i=1}^n x_{in}, \text{ where } \sum_{i=1}^n \sum_{j=1}^n x_{ij} = \sum_{j=1}^n x_j \quad (b)$$

The sums of the individual squares x^2 are

$$\sum_{i=1}^n x_{i1}^2, \sum_{i=1}^n x_{i2}^2, \dots, \sum_{i=1}^n x_{in}^2, \text{ where } \sum_{i=1}^n \sum_{j=1}^n x_{ij}^2 = \sum_{j=1}^n x_j^2 \quad (c)$$

The sums of squares calculated in accordance with (493) are

$$S_1, S_2, \dots, S_n, \text{ where } \sum_{i=1}^n S_i = S \quad (d)$$

The degrees of freedom are

$$\left. \begin{aligned} N_1 - 1, N_2 - 1, \dots, N_n - 1, \dots, N_n - 1, \\ (\text{symbolized by } v_1, v_2, \dots, v_n, \dots, v_n) \\ \text{where } \sum_{i=1}^n (N_i - 1) = N - n = v = \sum_{i=1}^n v_i \end{aligned} \right\} \quad (e)$$

The means $\bar{x}_1, \bar{x}_2, \dots, \bar{x}_n$ are defined by (491) (f)

and the variances $s_1^2, s_2^2, \dots, s_n^2$ by (492) (g)

17A. Testing variances

The hypothesis $\sigma_1^2 = \sigma_2^2 = \dots = \sigma_n^2$ is tested by m of BAILEY'S test²⁵.

An estimate of the common variance σ^2 is

$$s^2 = S/v \quad \left\{ \begin{aligned} s, v \text{ and } N \text{ from (620d, e and a)} \\ \text{where } v = N - n \end{aligned} \right. \quad (f)$$

The test statistic for s^2 is

$$\left. \begin{aligned} 2.3026 \left(v \log s^2 - \sum_{i=1}^n v_i \log s_i^2 \right) / k, \\ s^2 \text{ from (621), } v, v_i \text{ and } s_i^2 \text{ from (620e and g)} \end{aligned} \right\} \quad (a)$$

where

$$k = 1 + \left(\sum_{i=1}^n \frac{1}{v_i} - \frac{1}{v} \right) / (3(n-1)), \text{ and } v_i \text{ from (620e) } (b)$$

When $v_1 = v_2 = \dots = v_n = v$, (622a and b) become

$$2.3026 v \left[\log s^2 - (1/n) \sum_{i=1}^n \log s_i^2 \right] / k; \text{ see (a)} \quad (c)$$

and

$$k = 1 + (n+1)/3v, \text{ see (b)} \quad (d)$$

The significance limit for the test statistics (622a) and (622c) found from the χ^2 distribution with degrees of freedom $v = n - 1$ (tables on pages 36-39, $2\alpha = 1/\alpha$). If the test statistic *exceeds* the significance limit, then we may suspect that population with discrepant variances are among those being compared. If the test statistic is *smaller* than the limit, then in accordance with (6i) it can be assumed that all the populations have the same variance. In this case the means can be further tested as described in section 17B below.

17B. Testing means: Simple analysis of variance

In testing the hypothesis $\mu_1 = \mu_2 = \dots = \mu_n$ the following tabulation is first made [cf. also (420)]

	Sums of squares	Degrees of freedom	Variance
Variance between the samples	S_2	$n - 1$	$s_2^2 = S_2 / (n - 1)$
Variances within the samples	S_1	$N - n$	$s_1^2 = S_1 / (N - n)$
Total	S_T	$N - 1$	$s_T^2 = S_T / (N - 1)$

$$\text{where } S_2 = \sum_{i=1}^n N_i (\bar{x}_i - \bar{x})^2 = \sum_{i=1}^n \left(\sum_{j=1}^n x_{ij} \right)^2 / N_i - \left(\sum_{j=1}^n x_j \right)^2 / N \quad (a)$$

$$S_2 = S - \left[\text{from (620d)} \right] = S_T - S_1 \quad (b)$$

$$S_T = S_1 + S_2 = \sum_{i=1}^n x_i^2 - \left(\sum_{i=1}^n x_i \right)^2 / N \quad (c)$$

$$\text{and } v = \left(\sum_{i=1}^n x_i \right)^2 / N \quad (d)$$

In (624) a check is made by means of the two identities in (a), (b) and (c)

In (623), s_2^2 represents the dispersion of the sample means \bar{x} around the common mean \bar{x} , s_1^2 the dispersion of the individual values around the sample means. If all the samples originate from

The *t*-test (Student distribution)

Applicability: When σ is unknown and the degrees of freedom of $s \rightarrow N - 1 \leq 200$

Test quotient	Significance limit	
$\frac{ s - \mu }{s_{N-1}} \sqrt{N}; N \leq 201$	t_{N-1} , pages 32-35; $\alpha \rightarrow P, 2\alpha \rightarrow 2P$	(a)
$\frac{(s - \mu)^2 N}{s_{N-1}^2}; N \leq 201$	f_{N-1}^2 , page 42; $\alpha \rightarrow \frac{1}{2}P, 2\alpha \rightarrow P$; cf. (552)	(b)
$\frac{ s - \mu }{s_{N-1}}; N \leq 201$	$t_{N-1}/\sqrt{N} =$ confidence factor k_{α} , page 43	(c)

(599)

LORD's test based on the extreme range t^9

Applicability: Samples of size $N \leq 20$ (a) and $N > 20$ (b)

Test quotient	Significance limit	
$\frac{ s - \mu }{s_N - s_1}; N \leq 20;$ $s_1 < s_2 < \dots < s_N$	Page 53, middle left-hand table	(a)
$\frac{ s - \mu m}{[\sum (s_n - s_1)] A_{m,n}};$ $m \times n = N$	Page 49; $A_{m,n}$ page 48	(b)

(600)

$m =$ number of subgroups of size n (cf. section 14 A, page 170) in which $s_1 < s_2 < \dots < s_n$

The midrange test based on the extreme range t^{20}

Applicability: Samples of size $N \leq 10$

Test quotient	Significance limit	
$\frac{ s_N + s_1 - 2\mu }{s_N - s_1}; N \leq 10$	Page 53, upper right-hand table	(601)

WALSH test t^{21}

Applicability: Samples of size $4 \leq N \leq 14$ from any symmetrical population

Test quotient	Significance limit	
Page 53, lower right-hand table	Page 53, lower right-hand table	(602)

Note that while the use of (598b) and (599b) involves the squaring of $(s - \mu)$ it obviates extracting the square root of s^2 (provided s is not required). The use of (598c) and (599c) avoids the multiplication by \sqrt{N} , with the further advantage that the transition from t to r in using the table on page 43 is quite 'automatic'.

(600)-(602) are straightforward rapid tests [especially (601)] in which even s does not need to be calculated. Within the tabulated range their power is practically the same as that of (599). The WALSH test is suitable not only for normal but also for any other symmetrical distribution. In this case, the significance probability or N up to 8 is somewhat higher than that in the table. For $N > 8$ the values in the table are exact.

When a calculating machine is not available, multiplication is faster than division. In this event, the significance limit should be multiplied by the divisor of the test quotient in order to obtain the limit for the dividend.

Example 38. When t is the limit for $\frac{|s - \mu| \sqrt{N}}{s}$, then $t s$ is the limit for $|s - \mu| \sqrt{N}$.

16. The normally distributed population: Comparison of two samples

In comparing two samples, the following hypotheses concerning the parameters of the original populations must be taken into consideration:

$$\mu_1 = \mu_2 \quad (a) \quad (603)$$

16A. Comparison of variances

The test quotient for the hypothesis ($\sigma_1^2 = \sigma_2^2$) (4) (570), in which the larger of the two sample variances, always be made the numerator. This means that renumeration of the variances with respect to the indices of the t , necessary when s_1^2 (from sample 1) is smaller than s_2^2 , number of degrees of freedom v_1 in the tables on pages 40 is always that of the numerator of (570).

s_1^2 and s_2^2 must be calculated from (492). Their denominators are $v_1 = N_1 - 1$ and $v_2 = N_2 - 1$.

If the test quotient is smaller than the significance table on pages 40 and 41, then in accordance with (4) assumed that $\sigma_1^2 = \sigma_2^2$. In this case the means are compared by the procedure given in section 16B below. If the test quotient exceeds the significance limit F , then $\sigma_1^2 > \sigma_2^2$ (significance probability $\alpha = P$) or $\sigma_1^2 \neq \sigma_2^2$ (significance probability 2α) means are tested by the procedure given in section 16B.

16B. Comparison of means when $\sigma_1^2 = \sigma_2^2$

The following symbols are used here:

$$|\bar{x}_1 - \bar{x}_2| = d \text{ and } |\mu_1 - \mu_2| = \alpha$$

The estimate of the common standard deviation σ

$$s = \sqrt{\frac{S_1 + S_2}{N_1 + N_2 - 2}}; S_1 \text{ and } S_2 \text{ from (493)}$$

$$v_s = v_1 + v_2 = N_1 + N_2 - 2$$

The estimate of the standard deviation of the difference

$$s_d = s \sqrt{\frac{1}{N_1} + \frac{1}{N_2}}; s \text{ from (607)}; v_{s_d} = N_1 + N_2 - 2$$

If σ is known, s is replaced by σ in (608). If $N_1 = 1$, $s \sqrt{1 + 1/N_2}$, $v = N_2 - 1$; cf. also (452) and (583c) and (583d).

The test quotients for the hypotheses ($\mu_1 = \mu_2$) ($\sigma_1^2 = \sigma_2^2$) if σ is known or $v > 200$

$$d/s_d \text{ or } d/s_d; \text{ limit } |t_{\alpha}|, \text{ page 28}$$

when $v \leq 200$

$$d/s_d; \text{ limit } t_{\alpha}, \text{ pages 32-35}; \alpha = P, 2\alpha = 2P$$

or

$$d^2/s_d^2; \text{ limit } t_{\alpha}^2 [= F(1; v)], \text{ page 42}; \alpha = \frac{1}{2}P, 2\alpha = P$$

If the test quotient attains or exceeds the significance limit this is considered as evidence that $\mu_1 \neq \mu_2$. In this case desirable to test the hypothesis ($\mu_1 - \mu_2 = \alpha$) ($\sigma_1^2 = \sigma_2^2$)

The test quotients are obtained by replacing d in (609) by $|d - \alpha|$. If the quotient exceeds the significance limit, then this is considered as evidence that $\mu_1 - \mu_2 \neq \alpha$.

The confidence limits for α are

$$\text{two-sided} \quad \text{Prob}(d - t_{v, \alpha} \times s_d \leq \alpha \leq d + t_{v, \alpha} \times s_d) = 1 - 2\alpha \quad (a)$$

$$\text{one-sided with a single upper limit} \quad \text{Prob}(\alpha \leq d + t_{v, \alpha} \times s_d) = 1 - \alpha \quad (b)$$

If the test quotient in (609) is smaller than the significance limit then it may be assumed in accordance with (474) that $\sigma_1^2 = \sigma_2^2$. Since also $\sigma_1^2 = \sigma_2^2$, the conclusion may be drawn that samples 1 and 2 originated from the same population with and variance σ^2 . Estimates of these parameters are

$$\bar{x} = \frac{\sum_1^{N_1} x_1 + \sum_2^{N_2} x_2}{N_1 + N_2} = \frac{N_1 \bar{x}_1 + N_2 \bar{x}_2}{N_1 + N_2}$$

$$s^2 = \frac{S_1 + S_2 + \frac{(\sum_1^{N_1} x_1)^2}{N_1} + \frac{(\sum_2^{N_2} x_2)^2}{N_2} - \frac{(\sum_1^{N_1} x_1 + \sum_2^{N_2} x_2)^2}{N_1 + N_2}}{N_1 + N_2 - 1}$$

$$v_1 s_1^2 + v_2 s_2^2 + N_1 \bar{x}_1^2 + N_2 \bar{x}_2^2 - \frac{(N_1 \bar{x}_1 + N_2 \bar{x}_2)^2}{N_1 + N_2}$$

16C. Comparison of means when $\sigma_1^2 \neq \sigma_2^2$

If σ_1 and σ_2 are known, or $N_1 + N_2 > 200$, then

$$\sigma_d = \sqrt{\frac{\sigma_1^2}{N_1} + \frac{\sigma_2^2}{N_2}} \quad \text{and} \quad t_d = \sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}} \quad (614)$$

and the test quotients

$$\frac{d}{\sigma_d} \quad \text{and} \quad \frac{d}{t_d} \quad \text{or} \quad \frac{|d - \ell|}{\sigma_d} \quad \text{and} \quad \frac{|d - \ell|}{t_d} \quad (615)$$

have the same limits as (609a)

If σ_1 and σ_2 are unknown, then the test quotients

$$\frac{d}{t_d} \quad \text{and} \quad \frac{|d - \ell|}{t_d} \quad (616)$$

have the same limits as (609b)²², where

$$\left. \begin{aligned} t_d &= \sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}} & (a) \\ v &= \frac{1}{k^2/v_1 + (1-k)^2/v_2} & (b) \\ k &= \frac{N_2 s_1^2}{N_1 s_1^2 + N_2 s_2^2} & (c) \end{aligned} \right\} \quad (617)$$

(v_1 and v_2 are degrees of freedom of s_1 and s_2 respectively)

16D. Testing pair differences

differences is tested

Let A and B be the methods to be compared, $A_i - B_i = d_i$ the difference between the results given by these methods with the object i , N the total number of objects. A sample of size N of all

16D because of the non-independent nature of the samples

16E. Tests for two samples using the extreme ranges²³

(a) Two samples of the same size $N^* = N'' = N \leq 20$

$x_N^* - x_1^*$ and $x_N'' - x_1''$ are the extreme ranges of these samples, the test quotient is then

$$\frac{x_N^* - x_1^*}{x_N'' - x_1''} \quad (618)$$

(for limit see page 53, bottom left-hand table)

(b) Two samples of unequal size, or of the same size but larger than 20.

The samples are divided respectively into m' and m'' random subgroups of the same size n (cf. section 14A, page 170). The sum of all the extreme ranges of these subgroups from both samples is denoted by S_2 . The test quotient is then

$$\frac{S_2 - S_1}{S_2 \times A_{m,m'}} \quad \text{for } A_{m,m'} \text{ see page 49,} \quad (619)$$

17. The normally distributed population: Testing several samples

Given are n samples of sizes

$$N_1, N_2, \dots, N_n, \text{ where } \sum_{i=1}^n N_i = N \quad (620)$$

The sums of the individual values x are

$$\sum_{i=1}^{N_1} x_{1i}, \sum_{i=1}^{N_2} x_{2i}, \dots, \sum_{i=1}^{N_n} x_{ni}, \text{ where } \sum_{i=1}^N x_i = \sum_{i=1}^n \sum_{j=1}^{N_i} x_{ij} \quad (b)$$

The sums of the individual squares x^2 are

$$\sum_{i=1}^{N_1} x_{1i}^2, \sum_{i=1}^{N_2} x_{2i}^2, \dots, \sum_{i=1}^{N_n} x_{ni}^2, \text{ where } \sum_{i=1}^N x_i^2 = \sum_{i=1}^n \sum_{j=1}^{N_i} x_{ij}^2 \quad (c)$$

The sums of squares calculated in accordance with (493) are

$$S_1, S_2, \dots, S_n, \text{ where } \sum_{i=1}^n S_i = S \quad (d)$$

The degrees of freedom are

$$N_1 - 1, N_2 - 1, \dots, N_n - 1, \dots, N_n - 1, \quad (e)$$

(symbolized by $v_1, v_2, \dots, v_n, \dots, v_n$)

where $\sum_{i=1}^n (N_i - 1) = N - n = v = \sum_{i=1}^n v_i$

The means $\bar{x}_1, \bar{x}_2, \dots, \bar{x}_n, \dots, \bar{x}_n$ are defined by (491) (f)

and the variances $s_1^2, s_2^2, \dots, s_n^2, \dots, s_n^2$ by (492) (g)

17A. Testing variances

The hypothesis $\sigma_1^2 = \sigma_2^2 = \dots = \sigma_n^2 = \dots = \sigma_n^2$ is tested by means of BARTLETT's test²⁴,

An estimate of the common variance σ^2 is

$$s^2 = S/v \quad \left. \begin{aligned} & \text{where } v = N - n \end{aligned} \right\} S, v \text{ and } N \text{ from (420d, e and a)} \quad (621)$$

The test statistic for s^2 is

$$2.3026 \{v \log s^2 - \sum_{i=1}^n v_i \log s_i^2\} / k, \quad (a)$$

s^2 from (421), v_i and s_i^2 from (420e and g)

where

$$k = 1 + \left(\sum_{i=1}^n \frac{1}{v_i} - \frac{1}{v} \right) / 3(n-1), v \text{ and } v_i \text{ from (420e) (b)} \quad (622)$$

When $v_1 = v_2 = \dots = v_n = v$, (622a and b) become

$$2.3026 \{v \log s^2 - (1/n) \sum_{i=1}^n v \log s_i^2\} / k, \text{ see (a) (c)}$$

and

$$k = 1 + (n+1)/3, \text{ see (b) (d)}$$

The significance limit for the test statistics (622a) and (622c) is found from the χ^2 distribution with degrees of freedom $v = n - 1$

17B below

17B. Testing means: Simple analysis of variance

In testing the hypothesis $\mu_1 = \mu_2 = \dots = \mu_n = \mu$, the following tabulation is first made [cf. also (420)]:

	Sum of squares	Degrees of freedom	Variance
Variance between the samples	S_1	$n - 1$	$s_1^2 = S_1/(n - 1)$
Variances within the samples . . .	S_2	$N - n$	$s_2^2 = S_2/(N - n)$
Total . . .	S_T	$N - 1$	$s_T^2 = S_T/(N - 1)$

$$\left. \begin{aligned} \text{where } S_1 &= \sum_{i=1}^n N_i (\bar{x}_i - \bar{x})^2 = \sum_{i=1}^n \left(\frac{N_i}{N} \right)^2 \{N_i (\bar{x}_i - \bar{x})^2\} / N(n) \\ S_2 &= S - S_1 \text{ [from (420d)]} = S_T - S_1 \\ S_T &= S_1 + S_2 = \sum_{i=1}^n x_i^2 - \left(\sum_{i=1}^n x_i \right)^2 / N \\ \text{and } S_T &= \left(\sum_{i=1}^N x_i \right)^2 / N \end{aligned} \right\} \quad (624)$$

In (624) a check is made by means of the two identities (a), (b) and (c)

In (623), s_1^2 represents the dispersion of the sample means \bar{x}_i around the common mean \bar{x} , s_2^2 the dispersion of the individual values around the sample means. If all the samples originate from

the same population, so that $\mu_1 = \mu_2 = \dots = \mu_n = \mu$ (the hypothesis in the light of which the variances have been tested), then the variances s_1^2 and s_2^2 should be approximately of the same magnitude. If they are not, then among the samples are some with discrepant means, in which case s_2^2 must be greater than s_1^2 . The necessity of carrying out the appropriate F test is thus avoided when $s_1^2 \leq s_2^2$.

The test quotient is s_2^2/s_1^2 , limit F , pages 40-41; $\alpha = P$ with $s_1^2 > s_2^2$. } (625)

If the test quotient is smaller than the significance limit, then in accordance with (474) it can be assumed that all the samples originate from the same population. The estimates of their mean μ and variance σ^2 are

$$\bar{x} = (624d); s^2 = (621), \text{ with } v = N - n \quad (626)$$

with confidence and tolerance intervals constructed as described in (580)-(584).

If the test quotient attains or exceeds the significance limit F , then among the means there must be some of discrepant magnitude. Various methods of analysing this situation have been proposed²². Here that of DUNCAN²³ will be used.

The method is dependent on all samples having the same size N_0 . The standard deviation of a mean \bar{x}_i is first calculated

$$s_{\bar{x}_i} = \sqrt{s^2/N_0}; s^2 \text{ from (621)} \quad (627)$$

$$v_{\bar{x}_i} = N - n$$

The means \bar{x}_i are now ranked

$$\bar{x}_1 < \bar{x}_2 < \dots < \bar{x}_i < \dots < \bar{x}_n; \quad 1, 2, \dots, i, \dots, n = \text{ranks } O \quad (628)$$

and the n extreme ranges W_i corresponding to the degrees of freedom $v_{\bar{x}_i}$ and the ranks $O = 2, 3, \dots, n$ looked for in the table on page 50. Multiplication of these by the standard deviation of a mean $s_{\bar{x}_i}$ [cf. (627)] gives the extreme ranges of the means $W_{\bar{x}_i}$. Subtraction of these from the means \bar{x}_i gives the 'localized extreme ranges' $\bar{x}_i - W_{\bar{x}_i}$. The following conclusions can now be drawn:

The means falling in a 'localized extreme range' $\bar{x}_i - W_{\bar{x}_i}$ cannot be distinguished from each other significantly. } (629)

The means not distinguishable in (629) are underscored in the order of (628), with the result that

two means not underscored with a common line differ from one another significantly (significance probability α of the table). } (630)

Example 39. Given are 7 samples with the means \bar{x}_i shown below. $N_0 = 5$, $N = 35$, $s_v = 0.099$, $v_s = 28$. Significance probability $\alpha = 0.05$.

From (627) the estimated standard deviation of a mean is $s_{\bar{x}_i} = \sqrt{0.099/5} \approx 0.1407$. The extreme ranges W_i and $W_{\bar{x}_i} = W_i \times s_{\bar{x}_i}$ are given in the table below. The differences $\bar{x}_i - W_{\bar{x}_i}$ are then calculated up to the point where the corresponding underscoring matches or passes the lowest mean.

	1	2	3	4	5	6	7
\bar{x}_i	1.34	1.36	1.48	1.62	1.74	1.88	2.04
W_i		2.90	3.04	3.13	3.20	3.26	3.30
$W_{\bar{x}_i}$		0.408	0.428	0.440	0.450	0.459	0.464
$\bar{x}_i - W_{\bar{x}_i}$					1.290	1.421	1.576
(529)	1.34	1.36	1.48	1.62	1.74	1.88	2.04

The final result is given by (630): $2.04 > 1.34$ to 1.48 ; $1.88 > 1.34$ to 1.36 .

8. The normally distributed population: Regressions of the first kind

Discussion will be limited here to linear regression functions. The functional relationships between two or more variables are often more or less obscured by random influences. Thus the effect

of a dose of a drug, for example, will change in a certain way dose is increased. The effect will never be an exact function of dosage, however, and even in the same subject will fluctuate around a curve—the regression function—in a random manner. In statistical methods it is possible to estimate the parameters of regression function and the required variances.

Although in the above example the dose is not a random variable, the effect it brings about is a random variable. In this the regression is one of the first kind. In cases where both variables are random variables the regression is one of the second kind. Regression of the second kind can be treated as a regression of the first kind when the range of variation of the dependent variable as well as the points at which it is measured are arbitrarily determined beforehand.

In regressions of the first kind there is a single regression that of y on x , which is used for calculations in both directions from y to x as well as from x to y . Cf. also section 19, page

18A. Estimation of the parameters of the regression line [cf. also (298)-(311)]

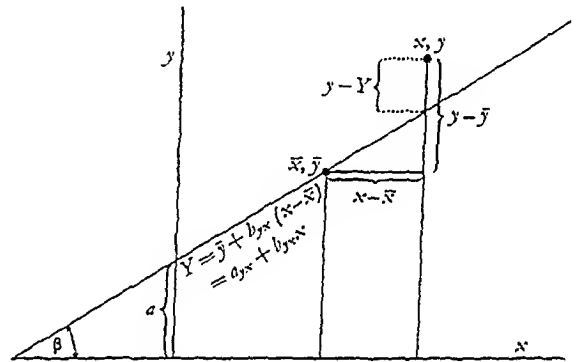


Fig. 35. Linear regression, ungrouped sample.

Ungrouped samples, two variables

Given are n pairs of observations x, y . x is the independent, n random variable, y the dependent, random variable.

Estimate Y of the regression line Y^*

$$\begin{aligned} Y &= \bar{y} + b_{yx}(x - \bar{x}) & (a) \\ &= a_{yx} + b_{yx}x & (b) \end{aligned} \quad (6)$$

where $a_{yx} = \bar{y} - b_{yx}\bar{x}$, with \bar{y} and \bar{x} calculated from (491), b_{yx} from (632).

Estimate b_{yx} of the regression coefficient b_{yx}

$$b_{yx} = \frac{s_{xy}}{s_x^2} = \frac{S_{xy}}{S_x} \quad (63)$$

with s_x^2 and S_x from (492) and (493). For s_{xy} see (633). b_{yx} is the tangent of the angle of inclination β_{yx} of the regression line. Cf. also (299).

Estimate s_{xy} of the covariance σ_{xy}

$$s_{xy} = \frac{\sum (x - \bar{x})(y - \bar{y})}{n - 1} = \frac{S_{xy}}{n - 1} \quad (63)$$

For S_{xy} see (634).

The calculation of S_{xy} is facilitated by the use of the following sums:

$$\begin{aligned} S_{xy} &= \sum (x - \bar{x})(y - \bar{y}) & (a) \\ &= \sum xy - \bar{x} \sum y & (b) \\ &= \sum xy - \bar{y} \sum x & (c) \\ &= \sum xy - \sum x \sum y / n & (d) \\ &= S_{xy}(n - 1) & (e) \end{aligned} \quad (634)$$

note $s^2_{y|x}$ of the residual variance $\sigma^2_{y|x}$

$$s^2_{y|x} = \frac{\Sigma(Y - y)^2}{n - 2} = \frac{S_{yy} - S_{yx}^2/S_{xx}}{n - 2} \quad (a) \quad (615)$$

$$= s^2_y(1 - r^2) \frac{n - 1}{n - 2} \quad (b)$$

S_{yy} and r^2 see (416) and (704)

$s^2_{y|x}$ is the variance of y when x is fixed. It is smaller than the variance s^2_y . In very rare cases (with very small correlation or regression coefficients) we can have

$$1 - r^2 \frac{n - 1}{n - 2} > 1, \text{ in which case } s^2_{y|x} > s^2_y$$

$$s^2_{y|x} = S_{yy} - \frac{S_{yx}^2}{S_{xx}} \quad (a) \quad (616)$$

$$= S_{yy} - \frac{S_{yx}^2}{S_{xx}} \quad (b)$$

$$= S_{yy}(1 - r^2) \quad (c)$$

and S_{yy} from (419), S_{yx} from (414), S_{xx} from (411); r^2 from (704). The remarks above on (435b) apply also to (616c).

estimate $s^2_{y|x}$ of the variance $\sigma^2_{y|x}$

$$s^2_{y|x} = s^2_y s^2_{y|x} \quad (a) \quad (617)$$

$$= (s^2_y/n) \times \frac{1 - r^2}{n - 2} = (S_{yy}/n) \times \frac{1 - r^2}{n - 2} \quad (b)$$

and s^2_y from (492); S_{yy} and S_{xx} from (411); r^2 from (704). The remarks above on (435b) apply also to (617b).

estimate $s^2_{y|x}$ of the variance $\sigma^2_{y|x}$ about the regression line \hat{Y} for given value of x

$$s^2_{y|x} = s^2_y \left\{ \frac{1}{n} + \frac{(x - \bar{x})^2}{S_{xx}} \right\} \quad v = n - 2 \quad (a) \quad (618)$$

$$= s^2_y \left\{ \frac{S_{yy}}{n} + \frac{(x - \bar{x})^2}{S_{xx}} \right\} \quad (b)$$

from (493), s^2_y from (431), S_{yy} from (417)

Special cases of (618) are

estimate $s^2_{y|x}$ of the variance $\sigma^2_{y|x}$ of the mean \bar{y}

$$s^2_{y|x} = s^2_y/n, \quad v = n - 2 \quad (619)$$

estimate $s^2_{y|x}$ of the variance $\sigma^2_{y|x}$ of the intercept a

$$s^2_{y|x} = s^2_y \left\{ \frac{1}{n} + \frac{\bar{x}^2}{S_{xx}} \right\} \quad v = n - 2 \quad (a) \quad (620)$$

$$= s^2_y \left\{ \frac{(\Sigma x^2)}{n} \right\} \quad (b)$$

$s^2_{y|x}$ from (437).

Example 40 Given is the sample

x	y	x	y	x	y
5.8	2.19	7.0	4.62	8.2	6.58
6.2	3.27	7.4	5.32	8.6	7.41
6.6	3.79	7.8	5.85	9.0	8.29

The y values in this example correspond to the empirical probits of example 31 in section 11 F, page 163

It follows that

$$\begin{aligned} \bar{x} &= 7.4 \text{ from (491)} \\ S_{xx} &= 9.6 \text{ from (493)} \\ \bar{y} &= 47.32/9 = 5.257 \text{ from (491)} \\ S_{yy} &= 280.651 - 248.798 = 31.853 \text{ from (493)} \\ s^2_y &= S_{yy}/8 = 3.981625, \quad s_y = 1.9954 \text{ from (492b)} \\ S_{yx} &= 367.620 - 350.168 = 17.452 \text{ from (434)} \\ s_{yx} &= 17.452/9.6 = 1.817916 \text{ from (432)} \\ s_{yx} &= 31.853/9.6 = 3.328333 \text{ from (436a or b)} \\ s^2_{y|x} &= 0.12677, \quad s_{y|x} = 0.35454 \text{ from (435a)} \\ s^2_{y|x} &= 0.0181/9.6 = 0.00188542, \quad s_{y|x} = 0.043421 \text{ from (437a)} \\ s^2_{y|x} &= 0.0181/9 = 0.00201, \quad s_{y|x} = 0.044843 \text{ from (437b)} \end{aligned}$$

$$s^2_{y|x} = 0.0181 \left(0.1 + \frac{(7.4)^2}{9.6} \right) = 0.105257, \quad s_{y|x} = 0.32443 \text{ from (440a)}$$

$$\hat{Y} = 5.257 + 1.817916(x - 7.4) \text{ from (431a)}$$

$$= -8.1948 + 1.8179x \text{ from (431b)}$$

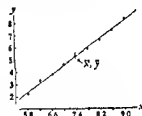


Fig 36 Probit line of example 40

A comparison of Figure 36 with Figure 30 (page 164) shows that

Grouped samples, two variables

Given are 1, 2, ..., k points of measurement (columns) x_i with m_1, m_2, \dots, m_k observations y_{ij} . x is the independent, non-random variable, y the dependent, random variable.

x	1	2	...	k	
y	11	21	...	$k1$	
	12	22	...	$k2$	
	$1j$	$2j$...	kj	
	$1m_1$	$2m_2$...	km_k	
	$\Sigma_{j=1}^m y_{1j}$	$\Sigma_{j=1}^m y_{2j}$...	$\Sigma_{j=1}^m y_{kj}$	
	Overall sum Σy_j , column sum Σy_j				(a, b)
	$\frac{(\Sigma y_{1j})^2}{m_1}$	$\frac{(\Sigma y_{2j})^2}{m_2}$...	$\frac{(\Sigma y_{kj})^2}{m_k}$	
	Overall sum $\Sigma (\Sigma y_j)^2/m_i$				(c)
$x y$	$x_1 \Sigma_{j=1}^m y_{1j}$	$x_2 \Sigma_{j=1}^m y_{2j}$...	$x_k \Sigma_{j=1}^m y_{kj}$	
	Overall sum $\Sigma x y$				(d) (641)
y^2	(11) ²	(21) ²	...	($k1$) ²	
	(12) ²	(22) ²	...	($k2$) ²	
	$(1j)^2$	$(2j)^2$...	$(kj)^2$	
	(1 m_1) ²	(2 m_2) ²	...	($k m_k$) ²	
	$\Sigma_{j=1}^m y_{1j}^2$	$\Sigma_{j=1}^m y_{2j}^2$...	$\Sigma_{j=1}^m y_{kj}^2$	
	Overall sum Σy_j^2 , column sum Σy_j^2				(e, f)
x^2	$m_1 x_1^2$	$m_2 x_2^2$...	$m_k x_k^2$	
	Overall sum Σx^2				(g)
	$m_1 x_1$	$m_2 x_2$...	$m_k x_k$	
	Overall sum Σx				(h)
$n = m$	$m_1 + m_2 + \dots + m_k$				(i)

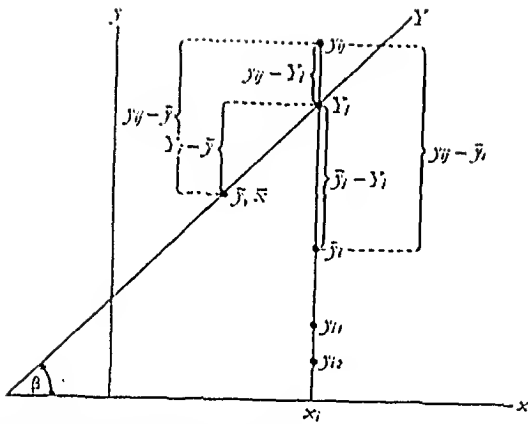


Fig. 37. Linear regression, grouped sample.

(641) allows the following to be calculated:

Column means

$$\bar{y}_i = (\Sigma y_i)/m_i = (641b)m_i \quad (642)$$

Sums of the squares of the deviations of the individual column values from the column means

$$S_{y_i} = \Sigma y_i^2 - (\Sigma y_i)^2/m_i = (641f) - (641b)^2/m_i \quad (643)$$

Overall mean

$$\bar{y} = (\Sigma y)/n = (641a)/(641i) \quad (644)$$

Mean of the independent variables

$$\bar{x} = (\Sigma x)/n = (641g)/(641i) \quad (645)$$

Sums of the squares of the deviations of x from \bar{x}

$$S_x = \Sigma x^2 - (\Sigma x)^2/n = (641h) - (641g)^2/(641i) \quad (646)$$

Sums of products

$$S_{xy} = \Sigma xy - \Sigma x \Sigma y/n = (641d) - (641g)(641a)/(641i) \quad (647)$$

Regression coefficient

$$b_{yx} = S_{xy}/S_x = (647)/(646) \quad (648)$$

Sums of the squares for variation within columns

$$S_1 = \sum_{i=1}^k S_{y_i} = \sum_{i=1}^k (643) \quad (649)$$

$$\left[= \sum_{i=1}^k \sum_{j=1}^{m_i} (y_{ij} - \bar{y}_i)^2 \right]$$

Sums of the squares of the deviations of the column means from the regression line Y'

$$S_2 = \Sigma (\Sigma y_i)^2/m_i - (\Sigma y)^2/n = S_3 \quad (650)$$

$$= (641c) - (641a)^2/(641i) - (651)$$

$$\left[= \sum_{i=1}^k m_i (\bar{y}_i - \bar{y})^2 \right]$$

S_3 from (651)

Sums of the squares of the deviations of the regression line from the overall mean

$$S_3 = b_{yx} S_{xy} = b_{yx}^2 S_x = S_{xy}^2/S_x = (648)(647) = (648)^2(646) \quad (651)$$

$$\left[= \sum_{i=1}^k m_i (\bar{y}_i - \bar{y})^2 \right]$$

Sums of the squares of the deviations of the individual values from the overall mean

$$S_y = \Sigma y^2 - (\Sigma y)^2/n = (641e) - (641a)^2/(641i) \quad (652)$$

$$\left[= \Sigma (y_{ij} - \bar{y})^2 \right]$$

Check:

$$S_1 + S_2 + S_3 = S_y \quad (653)$$

Sums of the squares of the residual variations

$$S_{y,x} = S_1 + S_2 = S_y - S_3 = (649) + (650) = (652) - (651) \quad (654)$$

Estimated variances

$$s_1^2 = S_1/(n-k) = (649)/(n-k); \nu = n-k \quad (655)$$

$$s_2^2 = S_2/(k-2) = (650)/(k-2); \nu = k-2 \quad (656)$$

$$s_3^2 = S_3 = (651); \nu = 1 \quad (657)$$

$$s_y^2 = S_y/(n-1) = (652)/(n-1); \nu = n-1 \quad (658)$$

$$s_{y,x}^2 = S_{y,x}/(n-2) = (654)/(n-2); \nu = n-2 \quad (659)$$

The equation of the regression line Y' and the estimated variances $s_{y,x}^2, s_1^2, s_2^2, s_3^2, s_y^2$ are obtained from (631), (637), (638), (639) and (640) by replacing b_{yx} by (648), $s_{y,x}^2$ by (659) and S_x by (646).

Example 41. Given is the sample

x	7	8	9
y	1.0 1.4 2.0 2.2	2.0 2.5 2.8 3.1 3.7 4.0	2.9 3.2 3.4 3.9 4.4
\bar{y}_i	6.6/4 = 1.65	18.1/6 = 3.016	17.8/5 = 3.56 from (642)
S_{y_i}	11.8 - 10.89 = 0.91	57.39 - 54.6016 = 2.7883	64.78 - 63.368 = 1.412 from (643)

$$n = 15 \text{ from (641i)}$$

$$\bar{y} = 42.5/15 = 2.83 \text{ from (644); } \bar{x} = (28 + 48 + 45)/15 = 8.06 \text{ from (645)}$$

$$S_x = (196 + 384 + 405) - (28 + 48 + 45)^2/15 = 8.93 \text{ from (646)}$$

$$S_{xy} = 46.2 + 144.8 + 160.2 - 8.06 \times 42.5 = 8.36 \text{ from (647)}$$

$$b_{yx} = 8.36/8.93 = 0.936567164 \text{ from (648)}$$

$$S_1 = 0.91 + 2.7883 + 1.412 = 5.1103 \text{ from (649)}$$

$$S_2 = 6.6^2/4 + 18.1^2/6 + 17.8^2/5 - 42.5^2/15 = S_3 = 0.607054728 \text{ from (650)}$$

$$S_3 = 0.936567164 \times 8.36 = 7.835945272 \text{ from (651)}$$

$$S_y = 133.97 - 42.5^2/15 = 13.553 \text{ from (652)}$$

Check: $5.1103 + 0.607054728 + 7.835945272 = 13.553$ from (653)

$$S_{x,y} = 5.1103 + 0.607055 = 5.717388 \text{ from (654)}$$

$$s_{y,x}^2 = 5.717388/13 = 0.439799; s_{y,x} = 0.663173 \text{ from (659)}$$

$$s_1^2 = 0.439799/8.93 = 0.0492312; s_1 = 0.221881 \text{ from (657a)}$$

$$Y' = 2.83 + 0.936567(x - 8.06) = -4.72164 + 0.936567x \text{ from (631)}$$

$$s_1^2 = S_1/12 = 0.425861 \text{ from (655); } s_2^2 = S_2/1 \text{ from (656); } s_3^2 = S_3 \text{ from (657)}$$

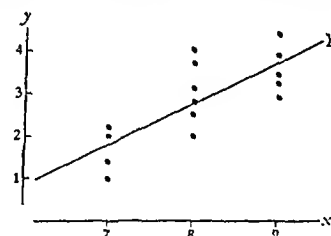


Fig. 38. Regression line of example 41.

18B. Testing the linearity of the regression function

With *ungrouped* samples, general departure from linearity of the regression function can be tested only by eye. The deviations $Y_i - y_i$ should give an impression of randomness and not show any systematic trend (cf. for example Fig. 29 [systematic deviations] with Fig. 30, right [apparently random deviations], on page 164).

With *grouped* samples an exact test is possible, namely by comparing the variance of the column means about the regression line with the variance within the columns.

Test quotient:

$$s_2^2/s_1^2 = (656)/(655); \text{significance limit } F \left\{ \begin{matrix} \nu_1 = k-2 \\ \nu_2 = n-k \end{matrix} \right\} \quad (660)$$

($2P = 2\alpha$, table on pages 40 and 41 [ν_1 of the table = ν_2 of the test quotient])

If the test quotient *attains* or *exceeds* the significance limit, then the regression function is quite possibly nonlinear (significance probability $2\alpha = 2P$). If the test quotient is *smaller* than the signifi-

limit, estimate plus G = upper limit). The parameters are intended to be included between these two limits

Confidence limits

$$\text{For } b_{yx}, \quad \left. \begin{aligned} b_{yx} \pm t_{\alpha/2} s_{b_{yx}}; v = n - 2 \leq 200 \\ b_{yx} \pm |t_{\alpha}| s_{b_{yx}}; v = n - 2 > 200 \end{aligned} \right\} s_{b_{yx}} = \sqrt{(637)} \quad (665)$$

For $\bar{Y} | x$:

$$\bar{y} \pm b_{yx}(x - \bar{x}) \pm t_{\alpha/2} s_{\bar{Y}|x}; v = n - 2 \leq 200 \\ \pm |t_{\alpha}| s_{\bar{Y}|x}; v = n - 2 > 200 \quad s_{\bar{Y}|x} = \sqrt{(638)} \quad (666)$$

For μ_y :

$$\bar{y} \pm t_{\alpha/2} s_y; v = n - 2 \leq 200 \\ \bar{y} \pm |t_{\alpha}| s_y; v = n - 2 > 200 \quad s_y = \sqrt{(639)} \quad (667)$$

For σ_{yx} :

$$s_{yx} \pm t_{\alpha/2} s_{s_{yx}}; v = n - 2 \leq 200 \\ s_{yx} \pm |t_{\alpha}| s_{s_{yx}}; v = n - 2 > 200 \quad s_{s_{yx}} = \sqrt{(640)} \quad (668)$$

(666) is a hyperbola (cf Fig 39)

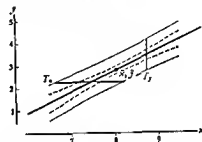


Fig 39 Confidence and tolerance limits for the regression of Figure 38
--- Confidence limits for \bar{Y} ——— Tolerance limits for \bar{Y} ——— Tolerance interval for $\bar{Y} | x$ T_y Tolerance interval for $X | y$

Tolerance limits for $\bar{Y} | x$

$$= \bar{y} + b_{yx}(x - \bar{x}) \pm t_{\alpha/2} s_{\bar{Y}|x}; v_1 = n - 2, \\ b_{yx} \text{ from (632) or (640)} \quad (669)$$

where

$$s_{\bar{Y}|x} = s_y \sqrt{1 + 1/n + (x - \bar{x})^2 / S_x}; v = n - 2 \quad (a) \\ = s_{s_{yx}} \sqrt{(1 + 1/n) S_x + (x - \bar{x})^2}; v = n - 2 \quad (b) \quad (670)$$

S_x from (493) or (646), $s_{s_{yx}} = \sqrt{(635)}$ or $\sqrt{(659)}$; $s_{b_{yx}} = \sqrt{(637a)}$, $s_{s_{yx}} = \sqrt{(640)}$ or $\sqrt{(645)}$

18F Estimation of x when y is given

$$x | y = \bar{x} + \frac{y - \bar{y}}{b_{yx}} \quad (671)$$

Confidence limits for the expected value of x , given y [solution from (666) for x]

$$\bar{x} + \frac{y - \bar{y}}{b_{yx}(1 - k^2)} \pm \\ \pm \frac{k}{b_{yx}(1 - k^2)} \sqrt{(1/n) b_{yx}^2 (1 - k^2) S_x + (y - \bar{y})^2} \quad (672)$$

where for ungrouped samples b_{yx} and S_x are obtained from (632) and (493), for grouped samples from (648) and (646)

$$k^2 = \frac{s_{\bar{Y}|x}^2}{b_{yx}^2}; v_1 = n - 2 \quad (673)$$

where $s_{\bar{Y}|x}^2 = (617)$

If $k^2 \leq 0.05$, then $1 - k^2$ can be taken as 1 in (672)

Tolerance limits for $x | y$ [solution from (669) for x]

(672) is used, but with $(1 + 1/n)$ in place of $1/n$ in the term under the root (674)

Example 44 In example 40, it is required to calculate x for $y = 5$ and the corresponding confidence and tolerance limits $x | y = 5$

$$x = 7.4 + \frac{5 - 5.257}{1.817916} = 7.2582 \text{ from (671)}$$

2. Testing the regression coefficient against zero

If the linearity of the regression function is not disproved by the

st statistics

$$\left. \begin{aligned} b_{yx}/s_{b_{yx}}; \text{significance limit } t, 2P = 2\alpha, \\ v = n - 2, \text{ pages 32-35} \end{aligned} \right\} (661)$$

$$s \text{ from (632) or (648), } s_{b_{yx}} = \sqrt{(637a)}$$

$$\left. \begin{aligned} b_{yx}^2/s_{b_{yx}}^2 = b^2 S_{yx}/s_{b_{yx}}^2; \text{significance limit } t^2, \\ P = 2\alpha, v = n - 2, \text{ page 42} \end{aligned} \right\} (662)$$

$$b^2 S_{yx} - t^2; s_{b_{yx}}^2; \text{significance limit null, } t^2 \text{ as in (662a) (b)}$$

With ungrouped samples, $b^2 S_{yx}$ is obtained from (632) and (624), with grouped samples from (631) $s_{b_{yx}}^2$ is obtained from (635) or (639)

If the correlation coefficient r has been calculated (cf section 9A, page 179), then

$$\text{when } r = 0, \text{ it follows that } b_{yx} \text{ (and } b_{xy}) = 0 \quad (663)$$

and vice versa. The hypothesis $b_{yx} = 0$ can be tested using r . Significance limit for $|r|$, see page 61, $v = n - 2$

If any of the test statistics in (661)–(663) attains or exceeds the corresponding significance limit, then b_{yx} differs significantly from zero. The above tests are special cases of (664a) for $b_{yx} = 0$

18D. Testing the difference between estimate and hypothetical value

Test quotients (absolute values should be used)

$$\left. \begin{aligned} (b_{yx} - b_{yx0})/s_{b_{yx}}; v = n - 2, s_{b_{yx}} = \sqrt{(637)} \quad (a) \\ (\bar{Y} - \bar{Y}_0)/s_{\bar{Y}|x}; v = n - 2, s_{\bar{Y}|x} = \sqrt{(638)} \quad (b) \\ (\bar{y} - \mu_y)/s_y; v = n - 2, s_y = \sqrt{(639)} \quad (c) \\ (s_{yx} - \sigma_{yx})/s_{s_{yx}}; v = n - 2, s_{s_{yx}} = \sqrt{(640)} \quad (d) \end{aligned} \right\} (664)$$

Example 43 [of (664a)] Comparison between the regression

line and the hypothetical line $y = 1.7123x - 11.8179$

$$\frac{1.8179 - 1.7123}{0.04342} = 2.432, v = 7$$

The corresponding significance limit $t_{\alpha/2, v}$, page 32, is 2.3646. The two regression coefficients, and therefore the regression lines, thus differ significantly

18E. Confidence and tolerance limits

Here only the formulae for the two-sided limits will be given, and these in the form of 'estimate $\pm G$ ' (estimate minus G = lower

Confidence limits: k^2 is first calculated from (673), giving

$$k^2 = \frac{2.3646^2 \times 0.00188542}{1.817916} = 0.003190; k = 0.05648$$

k^2 is less than 0.05, so that $1 - k^2$ can be taken as 1 in (672). For purposes of comparison, however, (672) is calculated with both values:

	Confidence limits	Tolerance limits
$1 - k^2 = 1$	7.2582 ± 0.0589 $= 7.1993 \text{ to } 7.3171$	7.2582 ± 0.5534 $= 6.7048 \text{ to } 7.8116$
$1 - k^2 = 0.996810$	7.2577 ± 0.0590 $= 7.1987 \text{ to } 7.3167$ from (672)	7.2577 ± 0.5545 $= 6.7032 \text{ to } 7.8122$ from (674)

18G. Comparison of two regression lines of the first kind

Given are the following ungrouped and grouped samples

$(x, y)_1$ with n_1	and $(x, y)_2$ and n_2	pairs of observations
\bar{x}_1	and \bar{x}_2	from (491) or (645)
\bar{y}_1	and \bar{y}_2	from (491) or (644)
S_{x_1}	and S_{x_2}	from (493) or (646)
S_{y_1}	and S_{y_2}	from (493) or (652)
$(S_{xy})_1$	and $(S_{xy})_2$	from (634) or (647)
$(S_{yx})_1$	and $(S_{yx})_2$	from (636) or (654)
$(s_{yx}^2)_1$	and $(s_{yx}^2)_2$	from (635) or (659)
$(b_{yx})_1 = b_1$	and $(b_{yx})_2 = b_2$	from (632) or (648)
Y_1	and Y_2	from (631)

In analogy with section 16 (page 172), the following hypotheses must be considered in comparing two linear regressions:

$$(\sigma_{y \cdot x}^2)_1 = (\sigma_{y \cdot x}^2)_2 \begin{cases} \mathbf{Y}_1 = \mathbf{Y}_2 & \text{(a) } \left\{ \begin{array}{l} \text{(675)} \\ \text{(676)} \end{array} \right. \\ \mathbf{Y}_1 \neq \mathbf{Y}_2 & \text{(b)} \end{cases} \quad \begin{cases} \mathbf{b}_1 = \mathbf{b}_2 \\ \mathbf{b}_1 \neq \mathbf{b}_2 \end{cases} \quad \begin{cases} \text{(a c)} \\ \text{(a d)} \end{cases}$$

$$(\sigma_{y \cdot x}^2)_1 \neq (\sigma_{y \cdot x}^2)_2 \begin{cases} \mathbf{Y}_1 = \mathbf{Y}_2 & \text{(a) } \left\{ \begin{array}{l} \text{(675)} \\ \text{(676)} \end{array} \right. \\ \mathbf{Y}_1 \neq \mathbf{Y}_2 & \text{(b)} \end{cases} \quad \begin{cases} \mathbf{b}_1 = \mathbf{b}_2 \\ \mathbf{b}_1 \neq \mathbf{b}_2 \end{cases} \quad \begin{cases} \text{(a c)} \\ \text{(a d)} \end{cases}$$

The hypothesis $(\sigma_{y \cdot x}^2)_1 = (\sigma_{y \cdot x}^2)_2$ is tested by means of the quotient

$$\frac{(s_{yx}^2)_1}{(s_{yx}^2)_2} \left\{ \begin{array}{l} \text{significance limit } F; \\ 2P = 2\alpha; \end{array} \right\} \left\{ \begin{array}{l} v_1 = n_1 - 2; \\ v_2 = n_2 - 2; \end{array} \right\} \quad \text{pages 40 and 41} \quad (677)$$

where the greater of the variances is given the index 1.

If the test quotient (677) is smaller than the significance limit, then (678)–(693) are valid; if the quotient attains or exceeds the significance limit, then (694)–(701) are valid.

If the test quotient (677) is smaller than the significance limit, then it is reasonable to assume that $(\sigma_{y \cdot x}^2)_1 = (\sigma_{y \cdot x}^2)_2$. The common variance $\sigma_{y \cdot x}^2$ of the two regression lines can then be estimated under the condition of (675) as

$$\bar{s}_{y \cdot x}^2 = \frac{(S_{yx})_1 + (S_{yx})_2}{n_1 + n_2 - 4}; v = n_1 + n_2 - 4 \quad (678)$$

(678) is used to test the hypothesis (675a), i.e., $b_1 = b_2$. The test quotient for the difference between the two regression coefficients under the conditions of (675) is

$$\frac{b_1 - b_2}{s_{Db}}; \text{significance limit } t; 2P = 2\alpha; v_t = n_1 + n_2 - 4 \quad (679)$$

$$\text{where } s_{Db}^2 = (678) \times \left(\frac{1}{S_{x_1}} + \frac{1}{S_{x_2}} \right) \quad (680)$$

If the test quotient (679) is smaller than the significance limit, then (681)–(693) are valid. If the quotient attains or exceeds the significance limit, then the regression lines are not parallel, i.e., $b_1 \neq b_2$. In other words,

if the test quotient (679) is smaller than the significance limit, then the two regression lines may be regarded as (681)

The estimate of the common residual variance $\sigma_{y \cdot x}^2$ when conditions of (675a) are fulfilled is

$$\bar{s}_{y \cdot x}^2 \approx (678); v = n_1 + n_2 - 4$$

$$\frac{(S_{yx})_1 + (S_{yx})_2 + \frac{(b_1 - b_2)^2}{1/S_{x_1} + 1/S_{x_2}}}{n_1 + n_2 - 3}; v = n_1 + n_2 - 3$$

The estimate \bar{b}_{yx} of the common regression coefficient b , the conditions of (675a) are fulfilled is

$$\bar{b}_{yx} = \frac{(S_{yx})_1 + (S_{yx})_2}{S_{x_1} + S_{x_2}}$$

The estimate $s_{b \cdot b}^2$ of the variance $\sigma_{b \cdot b}^2$ of the common regression coefficient when the conditions of (675a) are fulfilled is

$$s_{b \cdot b}^2 \approx \frac{(678)}{S_{x_1} + S_{x_2}}; v = n_1 + n_2 - 4 \quad (a)$$

$$\approx \frac{(682)}{S_{x_1} + S_{x_2}}; v = n_1 + n_2 - 3 \quad (b)$$

The two lines may be considered as identical [hypothesis (6) when the test quotient

$$\frac{\bar{b} - b}{s_{b \cdot b}} \left\{ \begin{array}{l} v = n_1 + n_2 - 4, \text{ when } s_{b \cdot b} = \sqrt{(687a)} \quad \bar{b} = (686) \\ v = n_1 + n_2 - 3, \text{ when } s_{b \cdot b} = \sqrt{(687b)} \quad \bar{b} = (683) \end{array} \right\}$$

is smaller than the significance limit t ($2P = 2\alpha$, pages 32–3)

$$\bar{b} = \frac{\bar{y}_1 - \bar{y}_2}{\bar{x}_1 - \bar{x}_2}$$

$$s_{b \cdot b}^2 \approx (678) \times K \quad (a) \\ \approx (682) \times K \quad (b) \quad \text{where } K = (688)$$

$$K = \frac{1}{(\bar{x}_1 - \bar{x}_2)^2} \left(\frac{1}{n_1} + \frac{1}{n_2} \right) + \frac{1}{S_{x_1} + S_{x_2}}$$

The two parallel regression lines do not coincide [hypot (675a d)] when the test quotient (685) attains or exceeds the significance limit. In this case the vertical and horizontal distances p_y and p_x are often of interest.

The vertical distance p_y and its confidence limits, when the conditions of (675a d) are fulfilled, are

$$p_y = |\bar{y}_1 - \bar{y}_2 - \bar{b}_{yx}(\bar{x}_1 - \bar{x}_2)|; \bar{b}_{yx} = (683)$$

Confidence limits for $p_{y \cdot x}$

$$\approx (689) \pm \frac{t_{2\alpha} \sqrt{(684a) \times [(1/n_1 + 1/n_2)(S_{x_1} + S_{x_2}) + (\bar{x}_1 - \bar{x}_2)^2]}}{v_t} \quad (a)$$

$$\text{where } v_t = n_1 + n_2 - 4$$

$$\approx (689) \pm \frac{t_{2\alpha} \sqrt{(684b) \times [(1/n_1 + 1/n_2)(S_{x_1} + S_{x_2}) + (\bar{x}_1 - \bar{x}_2)^2]}}{v_t} \quad (b)$$

$$\text{where } v_t = n_1 + n_2 - 3$$

The horizontal distance p_x and its confidence limits, when the conditions of (675a d) are fulfilled, are

$$p_x = \left| \bar{x}_1 - \bar{x}_2 - \frac{\bar{y}_1 - \bar{y}_2}{\bar{b}_{yx}} \right|; \bar{b}_{yx} \text{ from (683)} \quad (1)$$

Confidence limits for p_x

$$\approx \text{or } \approx \left| \bar{x}_1 - \bar{x}_2 - \frac{\bar{y}_1 - \bar{y}_2}{\bar{b}_{yx}(1 - k^2)} \right| \pm \frac{k}{\bar{b}_{yx}(1 - k^2)} \times \left[\sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2} \right) (\bar{b}_{yx})^2 (1 - k^2) (S_{x_1} + S_{x_2}) + (\bar{y}_1 - \bar{y}_2)^2} \right] \quad (6)$$

where $\bar{b}_{yx} = (683)$ and either $k = k_1 = (693a)$ or $k = k_2 = (693b)$. The approximation sign is for $k = k_1$, the equality sign for $k = k_2$.

$$k_1^2 = \frac{s_{b \cdot b}^2}{s_{b \cdot b}^2}; \left\{ \begin{array}{l} s_{b \cdot b}^2 = 684a; v_t = n_1 + n_2 - 4 \quad (a) \\ s_{b \cdot b}^2 = 684b; v_t = n_1 + n_2 - 3 \quad (b) \end{array} \right\} \quad (6)$$

When $k \leq 0.05$, the term $1 - k^2$ in (692) can be taken as 1.

If the test quotient (677) attains or exceeds the significance limit, then the two regression lines may be regarded as (694)

hypothesis (674a), that $b_1 = b_{12}$, is then tested by means of the quotient (679), where

$$t_{b_{12}}^2 = \frac{(s_{yy}^2)_1}{S_{y_1}} + \frac{(s_{yy}^2)_2}{S_{y_2}} \quad (674)$$

degrees of freedom $v_1 = (617b)$

with $k = \frac{(s_{yy}^2)_1 S_{x_2}}{(s_{yy}^2)_1 S_{x_1} + (s_{yy}^2)_2 S_{x_2}} \quad (674b)$

significance limit $t_{1-\alpha}$, with v_1 from (617b) and k from (674b)

If the test quotient (679) fitted to (694) is smaller than the significance limit, then it can be assumed that $b_1 = b_{12}$. The common regression coefficient is then

$$b_{yx} = \frac{\frac{(s_{xy})_1}{(s_{yy}^2)_1} + \frac{(s_{xy})_2}{(s_{yy}^2)_2}}{\frac{S_{x_1}}{(s_{yy}^2)_1} + \frac{S_{x_2}}{(s_{yy}^2)_2}} \quad (675)$$

with the estimated variance

$$s_{b_{yx}}^2 = \frac{1}{\frac{S_{x_1}}{(s_{yy}^2)_1} + \frac{S_{x_2}}{(s_{yy}^2)_2}} \quad (676)$$

Provided that the sample sizes n_1 and n_2 are large, the hypothesis (674a) that the two parallel regression lines are identical can be tested approximately by means of the quotient (685), where

$$t_{b_{12}}^2 = \frac{1}{(s_1 - s_2)^2} \left[\frac{(s_{yy}^2)_1}{n_1} + \frac{(s_{yy}^2)_2}{n_2} + (s_1 - s_2)^2 \right] \quad (685)$$

Significance limit $|t_{\alpha}|$, page 28

the vertical distance is

$$p_y = (689), \text{ where } \bar{y}_{yx} = (695) \quad (688)$$

with confidence limits

$$\bar{y}_{yx} \pm |t_{\alpha}| \times \sqrt{\frac{(s_{yy}^2)_1}{n_1} + \frac{(s_{yy}^2)_2}{n_2} + (s_1 - s_2)^2} \times (696) \quad (689)$$

the horizontal distance is

$$p_x = (691), \text{ where } \bar{x}_{yx} = (695) \quad (690)$$

with confidence limits

$$\bar{x}_{yx} \pm |t_{\alpha}| \times \sqrt{\frac{(s_{xx}^2)_1}{n_1} + \frac{(s_{xx}^2)_2}{n_2} + (s_1 - s_2)^2} \times \frac{k}{b_{yx}(1-k^2)} \quad (691)$$

$$t_{b_{12}}^2 = \frac{t_{b_{12}}^2 \times (696)}{(b_{yx})^2}, \quad e_{\alpha}, \text{ page 28, } t_{\alpha}^2 = \chi^2, \quad v = 1, \quad 1f, v = 2\alpha, \text{ page 36, } b_{yx} = (695)$$

When $\alpha \leq 0.05$, the term $1 - k^2$ in (701) can be taken as 1

Probit and logit regressions

With appropriate modifications, many of the formulae given in section 18 can be applied to probit and logit regressions. For further details the reader is referred to the literature. Probit regression^{11, 12, 24}, tables on pages 54 and 55. Logit regression²⁵, tables on pages 56 and 57.

19. The bivariate normal distribution: Regressions of the second kind

(Cf. introduction to section 18, page 174)

Given n pairs of observations x, y . Both x and y are random, normally distributed variables.

Regressions of the second kind are distinguished from those of the first kind by the existence of two regression lines

$$\begin{aligned} Y &= \bar{y} + b_{yx}(x - \bar{x}) & (a) \\ X &= \bar{x} + b_{xy}(y - \bar{y}) & (b) \end{aligned} \quad (702)$$

Estimates of the parameters of (702) and their variances are made by means of the appropriate formulae in section 18. In estimating the parameters of (702b), x and y in these formulae must be transposed.

19A. The correlation coefficient

A further parameter of regressions of the second kind is the

When the correlation coefficient is less than, equal to, or greater than zero, the two regression coefficients b_{yx} and b_{xy} are likewise less than, equal to, or greater than zero

The following relationships are valid for the correlation coefficient

$$r = \frac{s_{xy}}{s_x s_y} \quad (a)$$

and for its estimate

$$r = \frac{s_{xy}}{s_x s_y} = \frac{s_{xy}}{\sqrt{s_x^2 s_y^2}}, \quad s_x \text{ and } s_y \text{ from (493), } s_{xy} \text{ from (634)} \quad (b)$$

The square of the correlation coefficient r^2 is also known as the coefficient (or index) of determination

From (704) it follows that

$$r = \sqrt{\frac{s_{xy}}{s_x^2} \times \frac{s_{xy}}{s_y^2}} = \sqrt{b_{yx} \times b_{xy}} \quad (705)$$

From (115) it therefore follows that the correlation coefficient is also the geometric mean of the two regression coefficients b_{yx} and b_{xy} .

Under the hypothesis $\rho = 0$ when $n \rightarrow \infty$, the correlation coefficient is asymptotically related to the Student distribution. On the other hand,

$$\frac{r \sqrt{(n-2)}}{\sqrt{(1-r^2)}} \quad (706)$$

has a distribution of exact Student type with $v = n - 2$ degrees of freedom

The hypothesis can therefore be tested by means of the quotient $\frac{r \sqrt{(n-2)}}{\sqrt{(1-r^2)}}$, significance limit $|t_{\alpha}|$ for $n \leq 202$ (a) (707) $|t_{\alpha}|$ for $n > 202$ (b)

where $v = n - 2$

(706) does not need to be calculated for $v \leq 200$ since the significance limits for r can be taken directly from the table on page 61. They are based on the following formula identical with (707a)

$$|r| = \frac{t_{\alpha}}{\sqrt{v + t_{\alpha}^2}}; \quad v = n - 2 \quad (708)$$

If the test statistics from (706) or (708) attain or exceed the corresponding significance limits, then the correlation coefficient and the two regression coefficients differ significantly from zero. If $r \neq 0$, then the distribution of the sample correlation coefficient r is complicated in form. However, its distribution can be approximately normalized by means of R.A. FISHER's z -transformation, as follows:

$$\left. \begin{aligned} z &= \tanh^{-1} r = \frac{1}{2} \ln \frac{1+r}{1-r} \\ \text{and} \\ r &= \tanh z = \frac{e^{2z} - 1}{e^{2z} + 1} \end{aligned} \right\} \quad (709)$$

Cf. also Hyperbolic functions, page 140. Tables for (709a) are to be found on page 62 and for (709b) on pages 64 and 65.

The variance of z (2 variables x, y) is

$$\sigma_z^2 = \frac{1}{n-3}; \text{ cf. also page 62} \quad (710)$$

The expectation \bar{z} of z is

$$\left. \begin{aligned} \bar{z} &\approx \tanh^{-1} \bar{r} \\ &= \frac{\bar{r}}{2(n-1)} + \tanh^{-1} \bar{r} \end{aligned} \right\} \quad (711)$$

(711b) can as a rule be neglected (see below).

The following is derived from (709)-(711):

*Testing the difference between an estimate r and a hypothetical correlation coefficient r^**

Test quotient

$$\frac{|z - \bar{z}|}{\sigma_z} = |z - \bar{z}| \sqrt{n-3}; \quad z \text{ and } \bar{z} \text{ from (709a) and (711a)} \quad (712)$$

Significance limit $|c_\alpha|$, page 28, or $c_{2\alpha}$, page 31, lower table.

If the test quotient (712) is smaller than the significance limit, then there is no evidence that the population correlation coefficient differs from r^* .

*Confidence limits for r^**

$$\text{Prob} \left[\tanh \left(z - \frac{|c_\alpha|}{\sqrt{n-3}} \right) \leq r^* \leq \tanh \left(z + \frac{|c_\alpha|}{\sqrt{n-3}} \right) \right] \approx 1 - 2\alpha \quad (713)$$

Values for $\frac{|c_\alpha|}{\sqrt{n-3}}$ for $1 - 2\alpha = 0.95$ and 0.99 are given on page 63.

Comparison of two correlation coefficients r_1 and r_2

Testing the hypothesis $r_1 = r_2$ on the basis of the estimates r_1 and r_2 is effected by means of the following quotient:

$$\left. \begin{aligned} &\frac{|z_1 - z_2|}{\sqrt{\frac{1}{n_1-3} + \frac{1}{n_2-3}}}; \text{ significance limit } |c_\alpha|, \text{ page 28,} \\ &\text{or } c_{2\alpha}, \text{ page 31} \end{aligned} \right\} \quad (714)$$

If the test quotient (714) is smaller than the significance limit, then it can be assumed that $r_1 = r_2$. The estimate of the common correlation coefficient is then

$$\bar{r} = \tanh \bar{z} = \tanh \frac{(n_1-3)z_1 + (n_2-3)z_2}{n_1 + n_2 - 6} \quad (715)$$

$$\text{and } \sigma_{\bar{r}}^2 = \frac{1}{n_1 + n_2 - 6} \quad (716)$$

The confidence limits for the common correlation coefficient are

$$\left. \begin{aligned} &\text{Prob} [\tanh (\bar{z} - |c_\alpha| \sigma_{\bar{r}}) \leq \bar{r} \leq \tanh (\bar{z} + |c_\alpha| \sigma_{\bar{r}})] \\ &= 1 - 2\alpha; \text{ where } \sigma_{\bar{r}} = \sqrt{(716)} \end{aligned} \right\} \quad (717)$$

Comparison of several correlation coefficients

Given are k estimates r_1, r_2, \dots, r_k from k bivariate samples

$$\sum_1^k (n_i - 3) (z_i - \bar{z})^2; \text{ significance limit } \chi^2; 1 f_r = v_{\chi^2} = k; \text{ pages 36-39}$$

z_i and \bar{z} from (709a) and (711a).

If the hypothetical value is unknown, then its es

$$\bar{z} = \frac{\sum_1^k (n_i - 3) z_i}{\sum_1^k (n_i - 3)}$$

with variance

$$\sigma_{\bar{z}}^2 = \frac{1}{\sum_1^k (n_i - 3)}$$

Testing the hypothesis $r_1 = r_2 = \dots = r_k = \bar{r}$ is by means of the test statistic

$$\sum_1^k (n_i - 3) (z_i - \bar{z})^2; \text{ significance limit } \chi^2; 1 f_r = 2 v_{\chi^2} = k - 1; \text{ pages 36-39}$$

If the test statistic (721) is smaller than the significance limit, it can be assumed that $r_1 = r_2 = \dots = r_k = \bar{r}$. The common correlation coefficient \bar{r} is then approximately

$$\bar{r} \approx \tanh (\bar{z} - a \tanh \bar{z})$$

where \bar{z} is from (719) and

$$a = \frac{\sum_1^k \left(\frac{n_i - 3}{n_i - 1} \right)}{2 \sum_1^k (n_i - 3)}$$

The confidence limits for the common correlation coefficient are then approximately

$$\begin{aligned} \text{Prob} [\tanh (\bar{z} - a \tanh \bar{z} - |c_\alpha| \sigma_{\bar{r}}) \leq \bar{r} \leq \\ \leq \tanh (\bar{z} - a \tanh \bar{z} + |c_\alpha| \sigma_{\bar{r}})] \approx 1 - 2\alpha \end{aligned}$$

\bar{z} from (719), a from (723), $\sigma_{\bar{r}} = \sqrt{(720)}$, and significance page 28.

Examples, section 19A

Example 45. Given are $r = 0.3223$, $n = 34$. Does r differ ($2\alpha = 0.05$)? Since $v = 32$ and the corresponding limit (0.3388), the hypothesis $r = 0$ cannot be rejected.

Example 46. Given are $r = 0.613$, $n = 42$. Required a confidence limits for r^* :

$$z = 0.71371 \text{ (page 62)}$$

$$c_{\alpha} \sigma_z = 0.31385 \text{ (page 63)}$$

$$z \pm c_{\alpha} \sigma_z = 0.400 \text{ to } 1.027$$

$$\text{whence Prob } \left(\frac{0.380}{\text{page 64}} \leq r^* \leq \frac{0.773}{\text{page 64}} \right) = 0.95$$

Example 47

Given are		whence are obtained	
r_i	n_i	z_i	$n_i - 3$
0.555	12	0.62558	9
0.590	20	0.67767	17
0.670	15	0.81074	12
0.621	9	0.72663	6
0.733	26	0.93518	23
0.800	13	1.09861	10
		page 62	

$$\bar{z} = 63.73451/77 = 0.828 \text{ [from (719)]; } \tanh \bar{z} = 0.677$$

$$\chi^2 = 1.815; v = 6 - 1 = 5 \text{ [from (721)] page}$$

The 0.05 significance limit for χ^2 , $v = 5$, is 11.07 (page 36) it follows that the hypothesis $r_1 = r_2 = \dots = r_k = \bar{r}$ cannot be rejected.

$$a = 5.0734/154 = 0.0329 \text{ [from (723)]}$$

S_x and S_y are from (493), S_{xy} from (634), r from (704). Calculation is facilitated by using the relationship

$$r^2 = \frac{S_{xy}^2}{S_x S_y} \times S_{xy}$$

Comparison of a bivariate sample having means \bar{y} and \bar{x} with an independent pair of observations x, y , that is to say, testing the hypothesis that (x, y) come from the same (normal) population (\bar{x}, \bar{y}) , is made by means of the test statistic

$$\left. \begin{aligned} & \frac{n(n-2)}{2(n+1)(1-r^2)} \times \\ & \times \left[\frac{(x-\bar{x})^2}{S_x} + \frac{(y-\bar{y})^2}{S_y} - \frac{2S_{xy}(x-\bar{x})(y-\bar{y})}{S_x S_y} \right] \end{aligned} \right\} \quad (733)$$

Significance limits, degrees of freedom, etc. are all as in (732). (733) is a special case of (734) with $n_1 = 1$.

Simultaneous comparison of the means of two bivariate samples $(x, y)_1$ and $(x, y)_2$, that is to say, testing the hypothesis $(\mu_{y_1} = \mu_{y_2} | \mu_{x_1} = \mu_{x_2})$, is made by means of the following test statistic when $\sigma_{y_1}^2 = \sigma_{y_2}^2$, $\sigma_{x_1}^2 = \sigma_{x_2}^2$,

$$\left. \begin{aligned} & \frac{n_1 n_2 (n_1 + n_2 - 3)}{2(n_1 + n_2)(1-r^2)} \times \left\{ \frac{(\bar{x}_1 - \bar{x}_2)^2}{S_{x_1} + S_{x_2}} + \right. \\ & \left. + \frac{(\bar{y}_1 - \bar{y}_2)^2}{S_{y_1} + S_{y_2}} - \frac{2[(S_{xy})_1 + (S_{xy})_2](\bar{x}_1 - \bar{x}_2)(\bar{y}_1 - \bar{y}_2)}{(S_{x_1} + S_{x_2})(S_{y_1} + S_{y_2})} \right\} \end{aligned} \right\} \quad (734)$$

where

$$r^2 = \frac{[(S_{xy})_1 + (S_{xy})_2]^2}{(S_{x_1} + S_{x_2})(S_{y_1} + S_{y_2})}; \text{ for calculation cf. (732)} \quad (735)$$

Significance limit F ; $P = \alpha$; $v_1 = 2$, $v_2 = n_1 + n_2 - 3$; pages 40 and 41. Otherwise as in (732).

Approximate tests, preliminary to (734), can be made as follows:

Testing the hypothesis $\sigma_{y_1}^2 = \sigma_{y_2}^2$ and $\sigma_{x_1}^2 = \sigma_{x_2}^2$ from (605)

Testing the hypothesis $r_1 = r_2$ from (714)

For further discussion of tests of the above hypotheses see PEARSON and WILKS²⁸.

19D. Confidence and tolerance limits

100 $(1 - \alpha)\%$ confidence and tolerance limits are calculated by means of the formulae below on the basis of the estimates \bar{x} , \bar{y} , S_x , S_y , S_{xy} of a two-dimensional sample. b_{yx} and $s_{b_{yx}}$ are obtained from (632) and (637), b_{xy} and $s_{b_{xy}}$ likewise but with x and y transposed. Degrees of freedom of F : $v_1 = 2$, $v_2 = n - 2$; $1 - \alpha = 1 - P$; pages 40-41.

Confidence limits

$$\left. \begin{aligned} \mu_y | \mu_x = \bar{y} + b_{yx}(\mu_x - \bar{x}) \pm s_{b_{yx}} \sqrt{2FS_{x|n-(n-2)}(\mu_x - \bar{x})^2} \quad (a) \\ \mu_x | \mu_y = \bar{x} + b_{xy}(\mu_y - \bar{y}) \pm s_{b_{xy}} \sqrt{2FS_{y|n-(n-2)}(\mu_y - \bar{y})^2} \quad (b) \end{aligned} \right\} \quad (736)$$

(736a) and (736b) are identical confidence ellipses.

Tolerance limits

$$\left. \begin{aligned} \mathbf{X} | \mathbf{y} = \bar{y} + b_{yx}(x - \bar{x}) \pm s_{b_{yx}} \sqrt{2(n+1)FS_{x|n-(n-2)}(x - \bar{x})^2} \quad (a) \\ \mathbf{X} | \mathbf{y} = \bar{x} + b_{xy}(y - \bar{y}) \pm s_{b_{xy}} \sqrt{2(n+1)FS_{y|n-(n-2)}(y - \bar{y})^2} \quad (b) \end{aligned} \right\} \quad (737)$$

(737a) and (737b) are identical tolerance ellipses (see below).

The slopes of the main axes X_0 , Y_0 of the ellipses defined by (736) and (737) respectively, the so-called *orthogonal regression coefficients*, are

$$b_0 = \frac{1}{b_0} = \frac{S_y - S_x}{2S_{xy}} \pm \sqrt{1 + \left(\frac{S_y - S_x}{2S_{xy}} \right)^2} \quad (738)$$

where

$$k \begin{cases} = F/n(n-2) \text{ for confidence ellipse (736)} \\ = F(n+1)/n(n-2) \text{ for tolerance ellipse (737)} \end{cases} \quad (t)$$

Construction of ellipses

Rapid method: Calculation from (738) and (739) and tion from (315).

Exact method: From (736) or (737a) and/or (737b) in tion with (738) and (739), according to the accuracy requ

The equations of tangents to the confidence or tolerance parallel to the coordinate axes are:

$$\left. \begin{aligned} \text{Horizontal tangents: } y = \bar{y} \pm \sqrt{k S_y} \\ \text{Abscissae of the points of contact: } x = \bar{x} \pm b_{yx} \sqrt{k S_y} \end{aligned} \right\} \quad (a)$$

$$\left. \begin{aligned} \text{Vertical tangents: } x = \bar{x} \pm \sqrt{k S_x} \\ \text{Ordinates of the points of contact: } y = \bar{y} \pm b_{xy} \sqrt{k S_x} \end{aligned} \right\} \quad (b)$$

where

$$k \begin{cases} = 2F/n(n-2) \text{ for confidence ellipse (736)} \\ = 2F(n+1)/n(n-2) \text{ for tolerance ellipse (737)} \end{cases} \quad (a) \quad (b)$$

The lengths of the sides of the rectangle formed by these which circumscribes the ellipse arc:

$$\text{Horizontal sides} \quad (a)$$

$$l_h = 2\sqrt{k S_x}$$

$$\text{Vertical sides} \quad (b)$$

$$l_v = 2\sqrt{k S_y}$$

where $k = (742)$

Example 49. Given is the bivariate sample (Figs. 40 and

x	y	x	y	x	y	x
2.6	2.3	4.2	2.7	6.0	5.2	7.5
3.0	3.5	4.5	5.5	6.5	6.0	8.0
3.0	4.0	4.7	5.7	6.5	8.0	8.0
3.5	3.5	5.5	4.5	7.0	6.0	8.0
3.8	4.5	5.7	5.7	7.0	7.0	10.0

(a) The parameters are estimated.

(b) Using the formulae for the regression lines Y' and X' , orthogonal regression lines Y_0 and X_0 , for the tolerance ellipse $\mathbf{X}' | \mathbf{y}$ or $\mathbf{X} | \mathbf{y}$, and for the horizontal and vertical tangents latter, the lengths of the sides of the rectangle formed by the tangents and the lengths of the semi-axes of the ellipse are calculated.

(c) For purposes of comparison, the tolerance limits for $\mathbf{X}' | \mathbf{y}$ and $\mathbf{X} | \mathbf{y}$ are calculated using the appropriate formulae for regression of the first kind.

(d) A comparison is made of the tolerance limits for $\mathbf{X}' | \mathbf{y}$ of regressions of the second and first kind with $x = y = \bar{y}$.

(e) \bar{x} and \bar{y} are compared.

(a) Estimates of parameters

$$\begin{aligned} \bar{x} &= 115.0/20 = 5.75 & \bar{y} &= 111.3/20 = 5.565 \\ S_x &= 740.92 - 5.75 \times 115 & S_y &= 679.39 - 5.565 \times 11 \\ &= 79.67 & &= 60.0055 \\ s_x^2 &= 79.67/19 = 4.193158 & s_y^2 &= 60.0055/19 = 3.1581 \\ s_x &= 2.04772 & s_y &= 1.77713 \\ S_{xy} &= 700.90 - 5.75 \times 111.3 = 60.925 \text{ from (634)} \\ s_{xy} &= 60.925/19 = 3.206579 \\ r^2 &= 60.925^2 / (79.67 \times 60.0055) = 0.776435170 = (70 \\ 1 - r^2 &= 0.223564830 \\ r &= 0.881155 \\ b_{yx} &= 60.925/79.67 = 0.7647170 \text{ from (632)} \end{aligned}$$

$$\begin{aligned}
 -\frac{1}{b_1} &= (60.0055 - 79.67)/(2 \times 60.925) \\
 &\quad \pm \sqrt{1 + (-0.161382848)^2} = 0.85156 \text{ and} \\
 &\quad -1.17432 \text{ from (73b)} \\
 x &= 60.0055 \times 0.22356483 = 13.4151194 \text{ from (43c)} \\
 y &= 13.4151194/18 = 0.745284411 \text{ from (43a)} \\
 x &= 0.745284411/79.67 = 0.009354643 \text{ from (437a)} \\
 y &= 0.009354643 \times 0.00967224 \\
 x &= 79.67 \times 0.22356483 = 17.8114100 \text{ from (43c)*} \\
 y &= 17.8114100/18 = 0.989522777 \text{ from (43a)*} \\
 y &= 0.989522777/60.0055 = 0.01649053 \text{ from (437a)*} \\
 y &= 0.01649053 \times 0.00967224
 \end{aligned}$$

) Formulae

version lines

$$\begin{aligned}
 &= 5.565 + 0.7647(x - 5.75) = 1.679 + 0.7647x \text{ from (702a)} \\
 &= 5.75 + 1.0153(y - 5.565) = 0.0997 + 1.0153y \text{ from (702b)}
 \end{aligned}$$

$$\begin{aligned}
 x &= y - \bar{y} + b_1(x - \bar{x}) = 0.6685 + 0.8516x \\
 y &= \bar{y} - \bar{y} - \frac{1}{b_1}(x - \bar{x}) = 12.317 - 1.1743x
 \end{aligned}$$

range ellipse $[F_{1, 18}(2, 18) = 3.55, \text{ page 40}]$

$$\begin{aligned}
 \text{range limits for } X|y \\
 &= 5.565 \pm 0.7647(x - 5.75) \pm 0.09672 \times \\
 &\quad 593.94 - 18(x - 5.75)^2 \text{ from (737a)}
 \end{aligned}$$

$$\begin{aligned}
 \text{range limits for } X|y \\
 &= 5.75 + 1.0153(y - 5.565) \pm 0.12842 \times \\
 &\quad 447.34 - 18(y - 5.565)^2 \text{ from (737b)}
 \end{aligned}$$

horizontal tangents y and abscissae of the points of contact

$$\begin{aligned}
 y &= 5.565 \pm 4.99 = 0.58 \text{ and } 10.55 \\
 x &= 5.75 \pm 5.06 = 0.69 \text{ and } 10.81 \quad \left. \begin{array}{l} \text{from (741a) and (742b)} \end{array} \right\}
 \end{aligned}$$

vertical tangents x and ordinates of the points of contact

$$\begin{aligned}
 x &= 5.75 \pm 5.74 = 0.01 \text{ and } 11.49 \\
 y &= 5.565 \pm 4.39 = 1.18 \text{ and } 9.96 \quad \left. \begin{array}{l} \text{from (741b) and (742b)} \end{array} \right\}
 \end{aligned}$$

lengths of the sides of the resulting rectangle

$$\begin{aligned}
 \text{Horizontal sides } l_x &= 11.48 \\
 \text{Vertical sides } l_y &= 9.98 \quad \left. \begin{array}{l} \text{from (743) and (742b)} \end{array} \right\}
 \end{aligned}$$

lengths of the semi-axes of the ellipse

$$\begin{aligned}
 &= \sqrt{\frac{3.55 \times 21}{20 \times 18}} \times \\
 &\quad \sqrt{79.67 + 60.0055 \pm \sqrt{139.6755^2 - 4(4780.6382 - 60.925^2)}} \\
 &= 7.38 \text{ and } 1.83 \text{ from (739) and (740b)}
 \end{aligned}$$

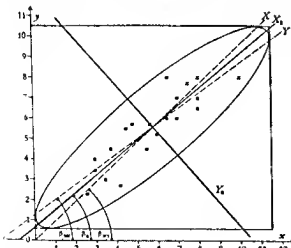


Fig. 40. Tolerance ellipse, example 49

* With x and y transposed(c) Tolerance limits for $X|y$ and $X|y$ calculated from the formulae for a regression of the first kind ($t_{18, 18, 18, 18} = 2.1009$, page 32)

$$\begin{aligned}
 X|y &= 5.565 + 0.7647(y - 5.75) \pm 0.2032 \times \\
 &\quad \sqrt{83.6535 + (y - 5.75)^2} \text{ from (449)}
 \end{aligned}$$

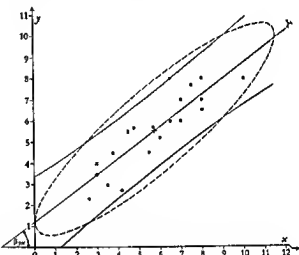
$$\begin{aligned}
 X|y &= 5.75 + 1.4070(y - 5.565) \pm 0.3739 \times \\
 &\quad \sqrt{45.4659 + (y - 5.565)^2} \text{ from (474)}
 \end{aligned}$$

(d) Tolerance limits for $X|y$ and $X|y$, with $x = \bar{x}$ and $y = \bar{y}$, calculated from the formulae for

Regression of second kind	Regression of first kind
$Y x = 5.565 \pm 2.3572$ from (737a)	5.565 ± 1.8585 from (469)
$X y = 5.75 \pm 2.7161$ from (737b)	5.75 ± 2.5213 from (474)

(e) Comparison of \bar{x} and \bar{y} ($t_{18, 18, 18, 18} = 2.09$)

$$\begin{aligned}
 &5.75 - 5.565 \\
 &\quad \sqrt{4.1932 + 3.1582 - 2 \times 3.2066} = 0.191 \text{ from (731)}
 \end{aligned}$$

The test statistic is smaller than the significance limit, so that the hypothesis $\bar{x} = \bar{y}$ cannot be rejectedFig. 41. Regression line of y on x , example 49. Tolerance limits calculated from the formulae for a regression of the first kind (hyperbolic) and second kind (ellipse)

20. The binomial distribution

(Cf also section 5, page 148)

20A. General

$$\begin{aligned}
 f(x) &= \hat{P}_x = \binom{N}{x} p^x q^{N-x} \\
 \hat{P}_1 &= \binom{N}{0} p^0 q^N = q^N \\
 \hat{P}_2 &= \binom{N}{1} p^1 q^{N-1} \\
 \hat{P}_N &= \binom{N}{N} p^N q^0 = p^N
 \end{aligned} \quad (244)$$

where $0 \leq p \leq 1$ and $q = 1 - p$ The individual probabilities \hat{P}_x of (244) correspond to the terms of the binomial series developed from $(q + p)^N$ [cf. (112)]. On the binomial coefficient $\binom{N}{x}$ cf. (100)-(106), page 136

From (244) follow the recursion formulae

$$\left. \begin{aligned} \dot{P}_{x+1} &= \dot{P}_x \times \frac{p}{q} \times \frac{N-x}{x+1} & (a) \\ \dot{P}_{x-1} &= \dot{P}_x \times \frac{q}{p} \times \frac{x}{N-x+1} & (b) \end{aligned} \right\} (745)$$

Example 50. Calculate all the individual probabilities \dot{P}_x for $p = 0.3$ and $N = 7$.

Calculations are made from (745a) starting from $x = 0$, $p/q = 3/7$.

$$\dot{P}_0 = \left(\frac{7}{10}\right)^7 = 0.0823543$$

$$\dot{P}_1 = \dot{P}_0 \times \frac{3}{7} \times \frac{7}{1} = \dot{P}_0 \times \frac{21}{7} = 0.2470629$$

$$\dot{P}_2 = \dot{P}_1 \times \frac{3}{7} \times \frac{6}{2} = \dot{P}_1 \times \frac{18}{14} = 0.3176523$$

$$\dot{P}_3 = \dot{P}_2 \times \frac{3}{7} \times \frac{5}{3} = \dot{P}_2 \times \frac{15}{21} = 0.2268945$$

A study of the series 21/7, 18/14, 15/21 at once reveals the regular manner in which the numerators and denominators of the recursion factors decrease and increase respectively. The further factors for calculating $\dot{P}_4, \dot{P}_5, \dots$ can therefore be assumed to be 2/28, 9/35, 6/42 and 3/49, giving

$$\dot{P}_4 = 0.0972405$$

$$\dot{P}_5 = 0.0250047$$

$$\dot{P}_6 = 0.0035721$$

$$\dot{P}_7 = 0.0002187$$

$$\text{Check: } \sum_{x=0}^N \dot{P}_x = 1$$

The individual probabilities for $N = 1, 2, \dots, 99, 100$ and $p = 0.01, 0.02, \dots, 0.49, 0.50$ can be obtained in a different manner using the tables on pages 70–77 (logarithms of binomial coefficients) and 78–84 (logarithms of powers of p and q).

Example 51. Calculate \dot{P}_1 for $p = 0.3$ and $N = 7$.

$$\log \binom{7}{1} = 0.84510 \quad (\text{page } 70)$$

$$\log p^1 = 0.47712 - 1 \quad (\text{page } 82)$$

$$\log q^6 = 0.07059 - 1 \quad (\text{page } 82)$$

$$\log \dot{P}_1 = 1.39281 - 2 = 0.3928 - 1$$

$$\dot{P}_1 = 0.2471 \quad (\text{page } 11)$$

For binomial coefficients with $N > 100$ see under 'Binomial Coefficients', page 136. For calculating powers of p and q , logarithms to 7 or more places should be used*.

The binomial distribution is a *discrete* distribution. It is *symmetrical* when $p = 0.5$, *asymmetrical* when $p \neq 0.5$.

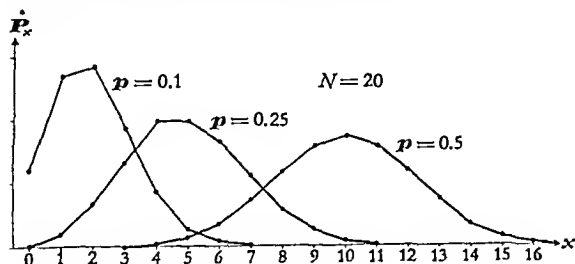


Fig. 42. Binomial distribution, $N = 20$, $p = 0.1, 0.25$ and 0.5 .

3. Parameters of the binomial distribution

As shown by (744), the binomial distribution is fully characterized by the probability p and the number of trials N , so that it can be represented by the expression 'binomial distribution ($p; N$)'. Mean and variance are respectively

$$\mu_x = Np = \text{expectation of (749)} \quad (746)$$

* Tables of $f(x)$ and the cumulative distribution $\sum_{x=0}^N f(x)$ for $N = 2, 3, \dots, 49$ and $p = 0.01, 0.02, \dots, 0.5$ are to be found in the literature 2, 4.

$$\sigma_x^2 = Npq = \sigma_{\mu_x}^2 = \text{expectation of (750)} \times \frac{N}{N-1}$$

For any given sample size N (N trials) the variance of the binomial distribution is greatest when $p = 0.5$, least when $p = 0$.

The best estimate of p from a sample of size N in which event E occurs x times is

$$\hat{p} = x/N$$

The following are derived from (746)–(748):

Estimate of μ_x

$$\hat{\mu}_x = N\hat{p} = x$$

Estimate of σ_x^2

$$\hat{\sigma}_x^2 = N\hat{p}\hat{q} = \frac{x(N-x)}{N}$$

The mean and variance of the *relative frequency* x/N are

$$\mu_{x/N} = \hat{p} = \text{expectation of (748)}$$

$$\sigma_{x/N}^2 = \frac{pq}{N} = \text{expectation of (753)} \times \frac{N}{N-1}$$

The corresponding estimates are

for the mean = (748)

$$\text{for the variance: } \hat{\sigma}_p^2 = \frac{\hat{p}\hat{q}}{N} = \frac{x(N-x)}{N^2} = \frac{1}{N^2} \hat{\sigma}_x^2$$

Example 52. In 64 trials the event x occurs 6 times. Estimate \hat{p} and $\hat{\sigma}_p^2$.

$$\hat{p} = 6/64 = 0.09375 \quad \text{from (748)}$$

$$\hat{\sigma}_x^2 = 0.09375 \times 58 = 5.4375 \quad \text{from (750)}$$

$$\hat{\sigma}_p^2 = 5.4375/64^2 = 0.001327515 \quad \text{from (753)}$$

20C. Cumulative probabilities of the binomial distribution

The calculation of cumulative probabilities in discrete distributions has been dealt with fully in section 5 (page 149). Here some practical applications are indicated.

Let p be the probability of the event E , q that of the event \bar{E} . \dot{P}_x is defined in (744).

The probability that the event E

- will occur exactly $x = k$ times is given by (370) (a)
- will *not* occur exactly $x = k$ times is given by (371) (b)
- will occur *at the most or less* than $x = k$ times is given by (372) (c)
- will occur *at least or more* than $x = k$ times is given by (373) (d)
- will occur at least $x = k$ times *but at the most* $x = r$ times ($k < r$) is given by (374) (e)
- will occur *less* than $x = k$ times *or more* than $x = r$ times ($k < r$) is given by (375) (f)

Examples of the calculation of probabilities of this kind are given in section 5, page 150. The following is an additional example.

Example 53. Let p be the probability of the occurrence of event E in a population. What size N must a sample have if the probability that the event E occurs *at least once* is p^* ?

From (754d) and (373) it follows that

$$\begin{aligned} \text{Prob}(x \geq 1) &= \sum_{x=1}^N \dot{P}_x \quad (\text{from } 373b) \\ &= 1 - \dot{P}_0 \quad (\text{from } 373a) \end{aligned}$$

In accordance with (744), $\dot{P}_0 = q^N$, whence

$$p^* = 1 - q^N$$

$$\text{that is, } N \sim \frac{\log(1 - p^*)}{\log q} = \frac{\log(1 - p^*)}{\log(1 - p)} \quad (75)$$

Application. Let the probability of throwing a six with a die be $1/6$. How many throws must be made in order to throw a six at least once with a probability $p^* \geq 0.99$?

From (755)

$$N = \frac{\log(1 - 0.99)}{\log(1 - 1/6)} = \frac{\log 0.01}{\log 5/6} \sim \frac{-2}{-0.0792} = 25.25$$

It follows that 26 throws must be made in order that, with a probability $p^* \approx 0.99$, at least one six will be thrown (with 25 throws p^* would be a little under 0.99)

20D. The binomial and the normal distribution

As shown by Figure 42, with $p = 1/2$, the binomial distribution closely resembles the normal distribution even with fairly small samples. This is not the case with more extreme values of p (cf. $p = 0.1$). As shown by Figure 43, however, with increasing sample size the binomial distribution approximates to the normal distribution even with more extreme values of p . In other words

With increasing sample size N the binomial distribution (p, N) tends toward the normal distribution (Np, \sqrt{Npq}). The closer p lies to 0.5, the greater is this tendency.

$$\binom{N}{x} p^x q^{N-x} \sim \frac{1}{\sqrt{2\pi Npq}} e^{-\frac{1}{2} \frac{(x - Np)^2}{Npq}} \quad (756)$$

as $N \rightarrow \infty$

With large sample sizes N , in accordance with the definitions

$$\text{Prob}(x \leq x_p) = \sum_{i=0}^x \binom{N}{i} p^i q^{N-i} = p$$

$\text{Prob}(z \leq z_p) = \int_{-\infty}^z$ of the standardized normal distribution

it follows from (756) that

$$\text{Prob}(x \leq x_p) \sim \text{Prob}(z \leq z_p) \quad (757)$$

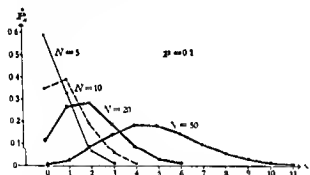


Fig 43 Binomial distribution, $p = 0.1$, $N = 5, 10, 20, 50$

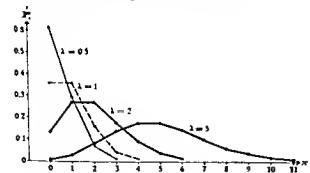


Fig 44 Poisson distribution, $\lambda = 0.5, 1, 2, 5$

where

$$z_p = \frac{x_p - Np}{\sqrt{Npq}}, \quad (\text{for } z \text{ see page 28, right hand table}) \quad (758)$$

or

$$x_p = Np + z_p \sqrt{Npq}, \quad (\text{for } z \text{ see page 28, left-hand table}) \quad (759)$$

With smaller samples, the transformations (757) and (758) can be improved by using the so-called correction for continuity. In this case, $x + 1/2$ is used in place of x , whence

$$z_p = \frac{x_p + 1/2 - Np}{\sqrt{Npq}}; \quad (\text{for } z \text{ see page 28, right-hand table}) \quad (760)$$

$$x_p = Np - 1/2 + z_p \sqrt{Npq}; \quad (\text{for } z \text{ see page 28, left-hand table}) \quad (761)$$

From the definitions

$$\text{Prob}(x \geq x_p) = 1 - \text{Prob}(x \leq x_p - 1) = p^*$$

$$\text{Prob}(z \leq z_{1-p}) = \int_{-\infty}^{z_{1-p}} \phi(z) dz = 1 - p^*$$

it follows from (760) and (761) that

$$z_{1-p} = \frac{x_p - 1/2 - Np}{\sqrt{Npq}}, \quad (\text{for } z \text{ see page 28, right-hand table}) \quad (762)$$

$$x_{p^*} = Np + 1/2 + z_{1-p} \sqrt{Npq}, \quad (\text{for } z \text{ see page 28, left-hand table}) \quad (763)$$

Example 54. Given the binomial distribution ($p = 0.1, N = 40$), calculate the probabilities $\text{Prob}(x \leq 3) = p$ and $\text{Prob}(x \geq 6) = p^*$ using the approximate formulae (760)–(763)

$$z_p = \frac{3.5 - 4}{\sqrt{3.6}} = -0.264 \quad [\text{from (760)}]$$

$$p = 0.396 \quad (\text{by linear interpolation in right-hand table, page 28})$$

$$z_{1-p} = \frac{5.5 - 4}{\sqrt{3.6}} = 0.791 \quad [\text{from (761)}]$$

$$1 - p^* = 0.786$$

$$p^* = 0.214$$

The exact values of p and p^* , rounded off to 3 decimal places, are 0.423 and 0.206

Example 55. For the binomial distribution of example 54, calculate x_p for $p = 0.1$ and x_{p^*} for $p^* = 0.05$ using the approximate formulae (760)–(763)

$$\left. \begin{aligned} z_p &= -1.2816 \\ z_{1-p} &= 1.6449 \end{aligned} \right\} \text{page 28, left-hand table}$$

whence

$$x_p = 3.5 - 1.2816 \sqrt{3.6} = 1.07 \quad [\text{from (761)}]$$

$$x_{p^*} = 4.5 + 1.6449 \sqrt{3.6} = 7.62 \quad [\text{from (763)}]$$

Since x must be a whole number, this gives the results $x_p = 1$ and $x_{p^*} = 8$, which agree with the nearest exact values

A further and, if $p < q$, rather better approximation²³ is

$$z_p = 2 \left[\sqrt{(x_p + 1)q} - \sqrt{(N - x_p)p} \right] \quad (764)$$

$$x_p = p \left(N + 1 - \frac{z_p^2}{4} \right) + \frac{z_p^2}{4} q - 1 + z_p \sqrt{pq \left(N + 1 - \frac{z_p^2}{4} \right)} \quad (765)$$

where in (765) $z = z_p$

$$z_{1-p} = 2 \left[\sqrt{(x_{p^*} - 1)q} - \sqrt{(N - x_{p^*} + 1)p} \right] \quad (766)$$

$$x_{p^*} = p \left(N + 1 - \frac{z_{1-p}^2}{4} \right) + \frac{z_{1-p}^2}{4} q + z_{1-p} \sqrt{pq \left(N + 1 - \frac{z_{1-p}^2}{4} \right)} \quad (767)$$

where in (767) $z = z_{1-p}$

The meaning of the symbols in (764)–(767) is the same as that in (760)–(763)

Example 56 Calculate examples 54 and 55 in accordance with (764)–(767)

$$z_p = 2 \left(\sqrt{4 \times 0.9} - \sqrt{37 \times 0.1} \right) = -0.052$$

$$p = 0.479$$

$$z_{1-p} = 2 \left(\sqrt{6 \times 0.9} - \sqrt{35 \times 0.1} \right) = 0.906$$

$$p^* = 1 - 0.817 = 0.183$$

$$x_p = 0.979$$

$$x_{p^*} = 8.00$$

20E. The binomial and the Poisson distribution

As shown by Figure 43, with small values of p the binomial distribution closely resembles the Poisson distribution. The following rule of thumb should be noted:

$$\left\{ \begin{aligned} \binom{N}{x} p^x q^{N-x} &\approx \frac{e^{-\lambda} \lambda^x}{x!}, \text{ where } \lambda = Np \\ \text{if } \frac{Np}{x} &\approx 1 \end{aligned} \right\} \quad (768)$$

20F. Confidence limits and significance limits

(a) *Confidence limits for p* , tables on pages 85-103 (or significance limits for $p = x/N$, cf. example 17, page 156)

In N trials, the event E occurs $x = k$ times. According to CLOPPER and PEARSON²⁰, the confidence limits satisfying the equation

$$\text{Prob}(p_l < p < p_r | x = k, N) = 1 - 2\alpha; \alpha < 0.5$$

are the solutions of

$$\left\{ \begin{aligned} \sum_{x=k}^N \binom{N}{x} p_l^x (1-p_l)^{N-x} &= \alpha \text{ for } p_l & (a) \\ \sum_{x=0}^k \binom{N}{x} p_r^x (1-p_r)^{N-x} &= \alpha \text{ for } p_r & (b) \end{aligned} \right\} \quad (769)$$

For $x=0$ and $x=N$, only one-sided $1-\alpha$ limits are possible:

$$\left\{ \begin{aligned} \text{for } x=0 & \\ 0 \text{ and } p_r &= 1 - \text{antilog} \left(\frac{\log \alpha}{N} \right) & (a) \\ \text{for } x=N & \\ p_l &= \text{antilog} \left(\frac{\log \alpha}{N} \right) \text{ and } N & (b) \end{aligned} \right\} \quad (770)$$

For $x=0$ and $x=N$, the confidence limits for p given in the tables on pages 85-103 thus correspond not to $1-2\alpha$, but to $1-\alpha$ limits.

For $0 < x < N$ an exact solution of (769) is possible only by means of an iterative process. The tables on pages 85-98 were calculated in this way by computer.

Approximate solutions are

$$p_l, p_r = \frac{x \mp \frac{1}{2} + \frac{c^2}{2} \mp |c| \sqrt{(x \mp \frac{1}{2}) \left(1 - \frac{x \mp \frac{1}{2}}{N} \right) + \frac{c^2}{4}}}{N + c^2} \quad (771)$$

where $c = c_\alpha$, page 28, left-hand table,

or, if $x \leq N/2$

$$\left\{ \begin{aligned} p_l, p_r &= (A - B) \mp \sqrt{B[2 - (A - B) - A]} \\ \text{where} & \\ A_{p_l}, A_{p_r} &= \frac{x + \frac{1}{2} \mp \frac{1}{2} + \frac{c^2}{4}}{N + 1} \\ B_{p_l}, B_{p_r} &= \frac{c^2}{2} \left(\frac{x + \frac{1}{2} \mp \frac{1}{2}}{(N + 1)^2} \right) \end{aligned} \right\} \quad (772)$$

where $c = c_\alpha$, page 28, left-hand table.

With larger samples, $\mp \frac{1}{2}$ in (771) and (772) can be ignored. (771) is the solution of (760) and (762) for p , (772) that of (764) and (766). The tables on pages 99-103 were calculated from (772) (for $x > 4$). In practice, (771) and (772) will seldom be required since the size of the tables is sufficient for most cases.

B. Parametric forms the confidence intervals for p for all possible N . As shown by (744), the sizes $N=30$ and $N=10$.

ed by the probability p and the limits not contained in the represented by the expression 'binomial' follows (the examples s mean and variance are respectively

$$\mu_x = Np = \text{expectation of (749)} \quad (x = 0, \dots, N)$$

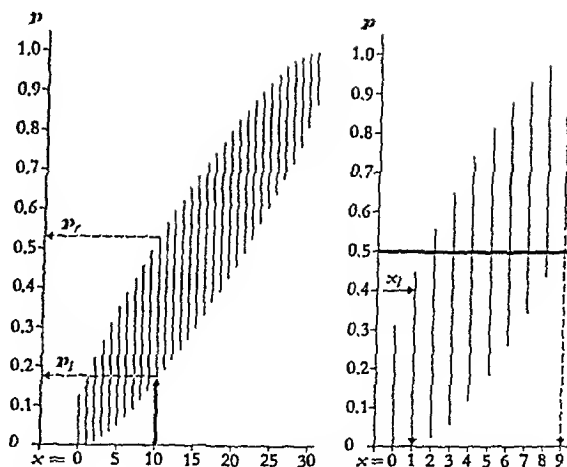


Fig. 45. Binomial distribution. Confidence limits for p ; $N=30$ and $N=10$

(1) x or $100 p_x (= 100 x/N)$ lies above the tabulated values in N column.

$N - x = x'$, or $100 - 100 p_x = 100 p'_x$, is first calculated and the corresponding limits $100 p'_l$ and $100 p'_r$ looked for in the table. The required limits are:

$$\left\{ \begin{aligned} \text{Lower } p_l &= 100 - 100 p'_r \\ \text{Upper } p_r &= 100 - 100 p'_l \end{aligned} \right\} \quad (77)$$

Example 57. $N=150$, $x=125$, $x'=150-125=25$, or $100 p'_x = 100 - 83.33 = 16.67$. For this the table gives $100 p'_l = 11.10$ and $100 p'_r = 23.64$, whence from (773) the required limits are 76.36 - 88.90.

(2) x or $100 p_x (= 100 x/N)$ lies between two values in an N column. $100 p_x$ lies between $100 p'_x$ and $100 p''_x$ ($p'_x < p''_x$).

The limits $100 p'_l$ and $100 p'_r$ for $100 p'_x$ and the limits $100 p''_l$ and $100 p''_r$ for $100 p''_x$ are looked for in the table:

$$\left\{ \begin{aligned} &\frac{100 p''_x}{100 p'_x} && \frac{100 p''_l}{100 p'_l} && \frac{100 p''_r}{100 p'_r} \\ &= B_l && = B_r \end{aligned} \right\} \quad (774)$$

If the quotient $\frac{100 p_x - 100 p'_x}{100 p''_x - 100 p'_x} = A$

then the required limits are

$$\left\{ \begin{aligned} 100 p_l &= 100 p'_l + (A \times B_l) \\ 100 p_r &= 100 p'_r + (A \times B_r) \end{aligned} \right.$$

Example 58. $N=500$, $x=427$, $100 p_x = 85.40$

$$\left\{ \begin{aligned} 100 p''_x &= 86.00 && 100 p''_l &= 82.64 && 100 p''_r &= 88.92 \\ 100 p'_x &= 84.00 && 100 p'_l &= 80.48 && 100 p'_r &= 87.10 \\ \text{Difference} &= 2.00 && &= 2.16 && &= 1.82 \end{aligned} \right.$$

$$\left\{ \begin{aligned} 100 p_x - 100 p'_x &= 85.40 - 84.00 = 1.40 \\ A &= 1.40 / 2.00 = 0.70 \end{aligned} \right.$$

$$\left\{ \begin{aligned} 100 p_l &= 80.48 + (0.7 \times 2.16) = 81.99 = 82.0 \\ 100 p_r &= 87.10 + (0.7 \times 1.82) = 88.37 = 88.4 \end{aligned} \right.$$

(3) N lies between N_1 and N_2 ($N_1 < N < N_2$). For $100 p_x (= 100 x/N)$ interpolation is made in column N_1 to give the limits $100 p_l^*$ and $100 p_r^*$, in column N_2 to give the limits $100 p_l^{**}$ and $100 p_r^{**}$, in accordance with (774). The required limits are then

$$\left\{ \begin{aligned} 100 p_l &= 100 p_l^* + \frac{N - N_1}{N_2 - N_1} (100 p_l^{**} - 100 p_l^*) \\ 100 p_r &= 100 p_r^* + \frac{N - N_1}{N_2 - N_1} (100 p_r^{**} - 100 p_r^*) \end{aligned} \right\} \quad (775)$$

Example 59. $N=270$, $x=22$, $100 p_x = 8.15$. $N=270$ lies between $N_1=250$ and $N_2=300$. The interpolated limits for $100 p_x = 8.15$ in accordance with (774) are in column

$$\left\{ \begin{aligned} N_2 &= 300 && 100 p_l^{**} &= 5.32 && 100 p_r^{**} &= 11.86 \\ N_1 &= 250 && 100 p_l^* &= 5.08 && 100 p_r^* &= 12.28 \end{aligned} \right.$$

$$\frac{N - N_1}{N_1 - N_2} = \frac{20}{50} = 0.4$$

$$00 p_1 = 5.08 + (0.4 \times 0.24) = 5.18 = \underline{5.2}$$

$$00 p_2 = 12.28 - (0.4 \times 0.42) = 12.11 = \underline{12.1}$$

4) N lies above 1000. For $100 p_2$ ($= 100 x/N$) the limits $100 p_1^*$ and $100 p_2^*$ are looked for in the column $N = 1000$. Then

$$\left. \begin{aligned} 100 p_2 - 100 p_1^* &= A \\ 100 p_2^* - 100 p_2 &= B \\ 100 p_1 &= 100 p_2 - A \sqrt{1000/N} \\ 100 p_2 &= 100 p_2 + B \sqrt{1000/N} \end{aligned} \right\} (776)$$

Example 60. Given are $N = 3000$ and $x = 69$, $100 p_2 = 2.30$. For $0 p_2 = 2.30$, column $N = 1000$ gives the limits $100 p_1^* = 1.46$ and $0 p_2^* = 3.44$

$$A = 2.30 - 1.46 = 0.84$$

$$B = 3.44 - 2.30 = 1.14$$

$$\sqrt{1000/3000} = \sqrt{1/3} \approx 0.577$$

$$100 p_1 = 2.3 - (0.84 \times 0.577) = 1.82 = \underline{1.8}$$

$$100 p_2 = 2.3 + (1.14 \times 0.577) = 2.96 = \underline{3.0}$$

(b) *Significance limits for x* , tables on pages 104-106 (or confidence limits for Np)

To find the significance limits for x , tables on pages 104-106 (or confidence limits for Np)

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(c) *Distribution-free tolerance limits for continuous distributions*, table on page 128 (cf. also sections 8C, page 155, and 10F, page 161)

The values of the sample sizes N in this table have been calculated by an iterative process based on a formula of WILKS²¹, so that

$$\sum_{i=1}^N \frac{\binom{N}{i} \beta_p^i (1 - \beta_p)^{N-i}}{i} \leq 1 - \beta_1 \quad (780)$$

The rounded-off values are based on the approximations²²

$$\left. \begin{aligned} N &\sim 1.03 x + 4.74 x^2 - 1 \quad \text{for } \beta_p = 0.90 \\ N &\sim 1.01 x + 9.75 x^2 - 1 \quad \text{for } \beta_p = 0.95 \\ N &\sim 1.00 x + 49.75 x^2 - 1 \quad \text{for } \beta_p = 0.99 \end{aligned} \right\} (781)$$

where x^* is so chosen that $1/x^*$ of the table on pages 36-39 equals $1 - \beta_1$ for $v = 4x$

The approximation to N obtained from (781) is very close to (780).

20G. Binomial distribution: Miscellaneous

(a) *Arc-sine transformation*, table on page 69 (cf. also 'Inverse trigonometric functions', page 139)

According to FREEMAN and TUKEY²³, the best transformation $x \rightarrow X$ for stabilizing the variance of the binomial distribution when $Np \geq 1$ is in most cases

$$\left. \begin{aligned} X &= \arcsin \sqrt{\frac{x}{N+1}} + \arcsin \sqrt{\frac{x+1}{N+1}} \\ \text{with a variance within } \pm 6\% \text{ of} \\ x^* &= \frac{1}{N + \frac{1}{2}} \left(\text{angle in} \right) \text{ or } \frac{821}{N + \frac{1}{2}} \left(\text{angle in} \right) \end{aligned} \right\} (782)$$

The mean \bar{X} of the values thus transformed is approximately $2 \arcsin \sqrt{p}$

This transformation can be used in variance analysis and other operations

(b) With a given p , how large must the sample size N be for the event E to occur at least x times with a probability p^* ? The solution of this problem for $x = 1$ is given in (783)

The simplest approximate solution for $x > 1$, on the basis of (766), is (when $p < q$)

$$N \sim \frac{1}{p} \left(\frac{e^{\epsilon}}{4} + x + \epsilon \sqrt{xq} \right) - 1 \quad (783)$$

where $\epsilon = \epsilon_p$.

21. The Poisson distribution

21A. General

E is a random event occurring over a long period of observation[†] an infinite number of times but in a relatively short time[†] (in general the observation unit t) only rarely. The probability that in an observation unit t the event will occur 0, 1, 2, ..., x times is then

$$f(x) = P_x = \frac{e^{-\lambda} \lambda^x}{x!} = \frac{e^{-\lambda} \lambda^0}{0!} \cdot \frac{e^{-\lambda} \lambda^1}{1!} \cdot \frac{e^{-\lambda} \lambda^2}{2!} \cdot \dots \quad (784)$$

e = base of natural logarithms; t = observation unit, for λ see (787), page 188

The simple calculation of several successive individual probabilities is from the recursion formula

$$P_{x+1} = P_x \times \frac{\lambda}{x+1} \quad (785)$$

[†] Time has been chosen as an example. The same arguments would apply, for instance, to surfaces and volumes

Example 61. Required are the 95% confidence limits for x for a sample of size $N = 10$ and a given $p = 0.5$

As shown by Figure 45, right, the lower limit x_1 is fixed by that confidence interval for p whose upper limit p_2 lies closest to the given p without exceeding it

The upper limit x_2 is fixed by that confidence interval for p whose lower limit p_1 lies closest to the given p without falling below it

In the table on page 85, $p_2 = 44/50$ is in accordance with (777a) and $p_1 = 55/50$ in accordance with (777b). The required limits for x are therefore $x_1 = 1$ and $x_2 = 9$

According to WILKS²¹, the above significance limits correspond to the distribution-free confidence limits for quantiles $Q(p)$ (cf. section 10F, page 161) when x_1 is replaced by $x_1 + 1$ and when p in the table is so chosen that it is of the same magnitude as p in $Q(p)$

In this connection it should be noted [cf. (382)] that the postulated significance probability is reached when x attains or exceeds in an outward direction from Np the limits x_1 or x_2

(one-tailed test) the sample originates from a population with $p > 0.05$ ($\alpha = 0.025$)

(two-tailed test) the sample originates from a population with $p \neq 0.05$ ($2\alpha = 0.05$)

On the basis of (760) and (762) or of (764) and (766) the following approximations are suitable for calculating the significance limits for x

$$x_1, x_2 = Np \mp \left(z_{\alpha} + \epsilon_{\alpha} \sqrt{Npq} \right) \quad (778)$$

(ϵ_{α} page 28, left-hand table)

or, if $p < q$

$$\left. \begin{aligned} x_1 + 1, x_2 &= p \left(N + 1 - \frac{1}{4} \right) + \\ &+ \frac{\epsilon_{\alpha}}{4} q \mp \epsilon_{\alpha} \sqrt{pq \left(N + 1 - \frac{1}{4} \right)} \end{aligned} \right\} (779)$$

(ϵ_{α} page 29, left-hand table)

As shown by Figure 43, with small values of p the binomial distribution closely resembles the Poisson distribution. The following rule of thumb should be noted:

$$\left. \begin{aligned} \binom{N}{x} p^x q^{N-x} &\approx \frac{e^{-\lambda} \lambda^x}{x!}, \text{ where } \lambda = Np \\ \text{if } \frac{Np}{Np} &\approx 1 \end{aligned} \right\} \quad (768)$$

20 F. Confidence limits and significance limits

(a) *Confidence limits for p* , tables on pages 85-103 (or significance limits for $p = x/N$, cf. example 17, page 156)

In N trials, the event E occurs $x = k$ times. According to CLOPPER and PEARSON²⁰, the confidence limits satisfying the equation

$$\text{Prob}(p_L < p < p_U | x = k, N) = 1 - 2\alpha; \alpha < 0.5$$

are the solutions of

$$\left. \begin{aligned} \sum_{x=k}^N \binom{N}{x} p_L^x (1-p_L)^{N-x} &= \alpha \text{ for } p_L & (a) \\ \sum_{x=0}^k \binom{N}{x} p_U^x (1-p_U)^{N-x} &= \alpha \text{ for } p_U & (b) \end{aligned} \right\} \quad (769)$$

For $x = 0$ and $x = N$, only one-sided $1 - \alpha$ limits are possible:

$$\left. \begin{aligned} \text{or } x = 0 & \\ 0 \text{ and } p_U &= 1 - \text{antilog} \left(\frac{\log \alpha}{N} \right) & (a) \\ \text{or } x = N & \\ p_L &= \text{antilog} \left(\frac{\log \alpha}{N} \right) \text{ and } N & (b) \end{aligned} \right\} \quad (770)$$

For $x = 0$ and $x = N$, the confidence limits for p given in the tables on pages 85-103 thus correspond not to $1 - 2\alpha$, but to $1 - \alpha$ limits.

For $0 < x < N$ an exact solution of (769) is possible only by means of an iterative process. The tables on pages 85-98 were calculated in this way by computer.

Approximate solutions are

$$p_L, p_U = \frac{x \mp \frac{1}{2} + \frac{c^2}{2} \mp |c|}{N + c^2} \sqrt{\left(x \mp \frac{1}{2} \right) \left(1 - \frac{x \mp \frac{1}{2}}{N} \right) + \frac{c^2}{4}} \quad (771)$$

where $c = c_\alpha$, page 28, left-hand table,

or, if $x \leq N/2$

$$\left. \begin{aligned} p_L, p_U &= (A - B) \mp \sqrt{B[2 - (A - B) - A]} \\ \text{where} & \\ A_{p_L}, A_{p_U} &= \frac{x + \frac{1}{2} \mp \frac{1}{2} + \frac{c^2}{4}}{N + 1} \\ B_{p_L}, B_{p_U} &= \frac{c^2}{2} \left(\frac{x + \frac{1}{2} \mp \frac{1}{2}}{(N + 1)^2} \right) \end{aligned} \right\} \quad (772)$$

here $c = c_\alpha$, page 28, left-hand table.

With larger samples, $\mp \frac{1}{2}$ in (771) and (772) can be ignored. (771) is the solution of (760) and (762) for p , (772) that of (764) and (766). The tables on pages 99-103 were calculated from (772) (if $x > 4$). In practice, (771) and (772) will seldom be required since the use of the tables is sufficient for most cases.

Figure 44 shows the confidence intervals for p for all possible values of the probability p and the sample size $N = 30$ and $N = 10$. The limits not contained in the expression 'binomial limits not contained in t' mean and variance are respectively

$$= Np = \text{expectation of (749)}$$

From (755)

$$N = \frac{\log(1 - 0.99)}{\log(1 - 1/6)} = \frac{\log 0.01}{\log 5/6} \sim \frac{-2}{-0.0792} \approx 25.25$$

It follows that 26 throws must be made in order that, with a probability $p^* \approx 0.99$, at least one six will be thrown (with 25 throws p^* would be a little under 0.99).

OD. The binomial and the normal distribution

As shown by Figure 42, with $p = 1/2$, the binomial distribution closely resembles the normal distribution even with fairly small samples. This is not the case with more extreme values of p (if $p = 0.1$). As shown by Figure 43, however, with increasing sample size the binomial distribution approximates to the normal distribution even with more extreme values of p . In other words:

With increasing sample size N the binomial distribution (p, N) tends toward the normal distribution (Np, \sqrt{Npq}). The closer p is to 0.5, the greater is this tendency.

$$\binom{N}{x} p^x q^{N-x} \rightarrow \frac{1}{\sqrt{2\pi Npq}} e^{-(x-Np)^2/2Npq} \quad (756)$$

as $N \rightarrow \infty$

With large sample sizes N , in accordance with the definitions

$$\text{Prob}(x \leq x_p) = \sum_{j=0}^x f_j = p$$

$$\text{Prob}(x \leq x_p) = \int_{-\infty}^{x_p} \text{of the standardized normal distribution}$$

it follows from (754) that

$$\text{Prob}(x \leq x_p) \approx \text{Prob}(z \leq z_p) \quad (757)$$

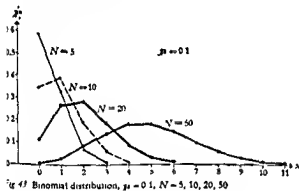


Fig. 42 Binomial distribution, $p = 0.1$, $N = 5, 10, 20, 50$

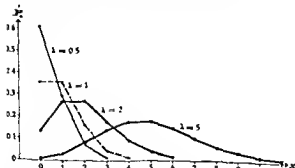


Fig. 43 Poisson distribution, $\lambda = 0.5, 1, 2, 5$

where

$$z_p = \frac{x_p - Np}{\sqrt{Npq}}, \quad (\text{for } z \text{ see page 28, right-hand table}) \quad (758)$$

or

$$x_p = Np + z_p \sqrt{Npq}, \quad (\text{for } z \text{ see page 28, left-hand table}) \quad (759)$$

With smaller samples, the transformations (757) and (758) can be improved by using the so-called correction for continuity. In this case, $x + 1/2$ is used in place of x , whence

$$z_p = \frac{x_p + 1/2 - Np}{\sqrt{Npq}}, \quad (\text{for } z \text{ see page 28, right-hand table}) \quad (760)$$

$$x_p = Np + z_p \sqrt{Npq}, \quad (\text{for } z \text{ see page 28, left-hand table}) \quad (761)$$

From the definitions

$$\text{Prob}(x \geq x_p) = 1 - \text{Prob}(x \leq x_p - 1) = p^*$$

$$\text{Prob}(x \leq x_{1-p}) = \int_{-\infty}^{x_{1-p}} = 1 - p^*$$

it follows from (760) and (761) that

$$z_{1-p} = \frac{x_{1-p} - 1/2 - Np}{\sqrt{Npq}}, \quad (\text{for } z \text{ see page 28, right-hand table}) \quad (762)$$

$$x_{p^*} = Np + 1/2 + z_{1-p} \sqrt{Npq}, \quad (\text{for } z \text{ see page 28, left-hand table}) \quad (763)$$

Example 54. Given the binomial distribution ($p = 0.1$, $N = 40$), calculate the probabilities $\text{Prob}(x \leq 3) = p$ and $\text{Prob}(x \geq 6) = p^*$ using the approximate formulae (760)–(763).

$$z_p = \frac{3.5 - 4}{\sqrt{3.6}} = -0.264 \quad (\text{from (760)})$$

$$p = 0.396 \quad (\text{by linear interpolation in right-hand table, page 28})$$

$$z_{1-p} = \frac{5.5 - 4}{\sqrt{3.6}} = 0.791 \quad (\text{from (761)})$$

$$1 - p^* = 0.796$$

$$p^* = 0.204$$

The exact values of p and p^* , rounded off to 4 decimal places, are 0.423 and 0.206.

Example 55. For the binomial distribution of Example 54, calculate x_p for $p = 0.1$ and x_{p^*} for $p^* = 0.04$ using the approximate formulae (760)–(763).

$$\left. \begin{aligned} z_p &= -1.2816 \\ z_{1-p} &= 1.6449 \end{aligned} \right\} \text{page 28, left-hand table}$$

whence

$$x_p = 3.5 - 1.2816 \sqrt{3.6} = 1.07 \quad (\text{from (760)})$$

$$x_{p^*} = 4.5 + 1.6449 \sqrt{3.6} = 7.62 \quad (\text{from (761)})$$

Since x must be a whole number, this gives the results $x_p = 1$ and $x_{p^*} = 8$, which agree with the nearest exact values.

A further and, if $p < q$, rather better approximation is

$$z_p = 2 \left[\sqrt{\frac{Np}{q}} \left(\frac{1}{2} - p \right) - \sqrt{\frac{Np}{q}} \right] \quad (764)$$

$$x_p = Np \left(1 + \frac{1}{4} \frac{1-p}{p} \right) + \frac{1}{4} q = 1 + \frac{1}{4} \sqrt{Npq} \left(\frac{1}{p} + 1 - \frac{1}{4} \right) \quad (765)$$

where in (765) $z = z_p$

$$z_{1-p} = 2 \left[\sqrt{\frac{Np}{q}} - \sqrt{\frac{Np}{q}} \left(\frac{1}{2} - p \right) \right] \quad (766)$$

$$x_{p^*} = Np \left(1 + \frac{1}{4} \frac{p}{1-p} \right) + \frac{1}{4} q = 1 + \frac{1}{4} \sqrt{Npq} \left(\frac{1}{1-p} + 1 - \frac{1}{4} \right) \quad (767)$$

where in (767) $z = z_{1-p}$

The meaning of the symbols in (764)–(767) is the same as that in (760)–(763).

Example 56. Calculate examples 54 and 55 in accordance with (764)–(767).

$$z_p = 2 \left(\sqrt{4 \times 0.9} - \sqrt{37 \times 0.1} \right) = -0.052$$

$$p = 0.479$$

$$z_{1-p} = 2 \left(\sqrt{6 \times 0.9} - \sqrt{35 \times 0.1} \right) = 0.906$$

$$p^* = 1 - 0.817 = 0.183$$

$$x_p = 0.979$$

or

20E. The binomial and the Poisson distribution

As shown by Figure 43, with small values of p the binomial distribution closely resembles the Poisson distribution. The following rule of thumb should be noted:

$$\left\{ \begin{aligned} \binom{N}{x} p^x q^{N-x} &\approx \frac{e^{-\lambda} \lambda^x}{x!}, \text{ where } \lambda = Np \\ \text{if } \frac{Np}{x} &\approx 1 \end{aligned} \right\} \quad (768)$$

20F. Confidence limits and significance limits

(a) *Confidence limits for p* , tables on pages 85-103 (or significance limits for $p \approx x/N$, cf. example 17, page 156)

In N trials, the event E occurs $x = k$ times. According to CLOPPER and PEARSON³⁰, the confidence limits satisfying the equation

$$\text{Prob}(p_l < p < p_r | x = k, N) = 1 - 2\alpha; \alpha < 0.5$$

are the solutions of

$$\left\{ \begin{aligned} \sum_{x=k}^N \binom{N}{x} p_l^x (1-p_l)^{N-x} &= \alpha \text{ for } p_l & (a) \\ \sum_{x=0}^k \binom{N}{x} p_r^x (1-p_r)^{N-x} &= \alpha \text{ for } p_r & (b) \end{aligned} \right\} \quad (769)$$

For $x=0$ and $x=N$, only one-sided $1-\alpha$ limits are possible:

$$\left\{ \begin{aligned} 0 \text{ and } p_r &= 1 - \text{antilog} \left(\frac{\log \alpha}{N} \right) & (a) \\ p_l &= \text{antilog} \left(\frac{\log \alpha}{N} \right) \text{ and } N & (b) \end{aligned} \right\} \quad (770)$$

For $x=0$ and $x=N$, the confidence limits for p given in the tables on pages 85-103 thus correspond not to $1-2\alpha$, but to $1-\alpha$ limits.

For $0 < x < N$ an exact solution of (769) is possible only by means of an iterative process. The tables on pages 85-98 were calculated in this way by computer.

Approximate solutions are

$$p_l, p_r = \frac{x \mp \frac{1}{2} \mp \frac{c^2}{2} \mp |c| \sqrt{\left(x \mp \frac{1}{2}\right) \left(1 - \frac{x \mp \frac{1}{2}}{N}\right) + \frac{c^2}{4}}}{N + c^2} \quad (771)$$

where $c = c_\alpha$, page 28, left-hand table,

or, if $x \leq N/2$

$$\left\{ \begin{aligned} p_l, p_r &= (A - B) \mp \sqrt{B[2 - (A - B) - A]} \\ \text{where} \\ A_{p_l}, A_{p_r} &= \frac{x + \frac{1}{2} \mp \frac{1}{2} + \frac{c^2}{4}}{N + 1} \\ B_{p_l}, B_{p_r} &= \frac{c^2}{2} \left(\frac{x + \frac{1}{2} \mp \frac{1}{2}}{(N + 1)^2} \right) \end{aligned} \right\} \quad (772)$$

where $c = c_\alpha$, page 28, left-hand table.

With larger samples, $\mp \frac{1}{2}$ in (771) and (772) can be ignored. (771) is the solution of (760) and (762) for p , (772) that of (764) and (766). The tables on pages 99-103 were calculated from (772) (for $x > 4$). In practice, (771) and (772) will seldom be required since the range of the tables is sufficient for most cases.

Figure 45 shows the confidence intervals for p for all possible values of x for sample sizes $N = 30$ and $N = 10$.

Interpolation and extrapolation for limits not contained in the tables on pages 99-103 are carried out as follows (the examples are all for 95% limits):

Four different situations will be considered, of which (1) can be

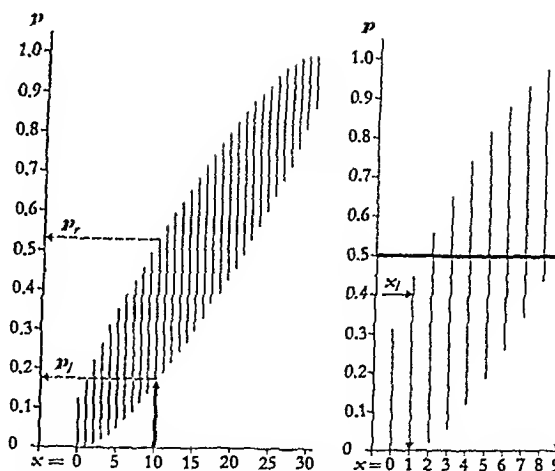


Fig. 45. Binomial distribution. Confidence limits for p ; $N = 30$ and $N = 10$.

(1) x or $100 p_x (= 100 x/N)$ lies above the tabulated values in N column.

$N - x = x'$, or $100 - 100 p_x = 100 p'_x$, is first calculated and the corresponding limits $100 p'_l$ and $100 p'_r$ looked for in the table. The required limits are:

$$\left\{ \begin{aligned} \text{Lower } p_l &= 100 - 100 p'_r \\ \text{Upper } p_r &= 100 - 100 p'_l \end{aligned} \right\} \quad (7)$$

Example 57. $N = 150$, $x = 125$. $x' = 150 - 125 = 25$, or $100 p'_x$ $100 - 83.33 = 16.67$. For this the table gives $100 p'_l = 11.10$ and $100 p'_r = 23.64$, whence from (773) the required limits are 76.36 and 88.90.

(2) x or $100 p_x (= 100 x/N)$ lies between two values in a column. $100 p_x$ lies between $100 p'_x$ and $100 p''_x$ ($p'_x < p_x < p''_x$).

The limits $100 p'_l$ and $100 p'_r$ for $100 p'_x$ and the limits $100 p''_l$ and $100 p''_r$ for $100 p''_x$ are looked for in the table:

$$\left\{ \begin{array}{ccc} 100 p''_x & 100 p'_x & 100 p'_x \\ 100 p'_x & 100 p'_l & 100 p'_r \\ (100 p''_x - 100 p'_x) & (100 p'_l - 100 p'_r) & (100 p''_r - 100 p'_r) \\ & = B_l & = B_r \end{array} \right\} \quad (774)$$

If the quotient $\frac{100 p_x - 100 p'_x}{100 p''_x - 100 p'_x} = A$

then the required limits are

$$\left\{ \begin{aligned} 100 p_l &= 100 p'_l + (A \times B_l) \\ 100 p_r &= 100 p'_r + (A \times B_r) \end{aligned} \right.$$

Example 58. $N = 500$, $x = 427$, $100 p_x = 85.40$

$$\left\{ \begin{array}{ccc} 100 p''_x = 86.00 & 100 p'_x = 82.64 & 100 p'_x = 88.92 \\ 100 p'_x = 84.00 & 100 p'_l = 80.48 & 100 p'_r = 87.10 \\ \text{Difference } 2.00 & 2.16 & 1.82 \end{array} \right.$$

$$\left\{ \begin{aligned} 100 p_x - 100 p'_x &= 85.40 - 84.00 = 1.40 \\ A &= 1.40 / 2.00 = 0.70 \end{aligned} \right.$$

$$\left\{ \begin{aligned} 100 p_l &= 80.48 + (0.7 \times 2.16) = 81.99 = 82.0 \\ 100 p_r &= 87.10 + (0.7 \times 1.82) = 88.37 = 88.4 \end{aligned} \right.$$

(3) N lies between N_1 and N_2 ($N_1 < N < N_2$). For $100 p_x (= 100 x/N)$ interpolation is made in column N_1 to give the limits $100 p_1^*$ and $100 p_2^*$, in column N_2 to give the limits $100 p_1^{**}$ and $100 p_2^{**}$, in accordance with (774). The required limits are then

$$\left\{ \begin{aligned} 100 p_l &= 100 p_1^* + \frac{N - N_1}{N_2 - N_1} (100 p_1^{**} - 100 p_1^*) \\ 100 p_r &= 100 p_2^* + \frac{N - N_1}{N_2 - N_1} (100 p_2^{**} - 100 p_2^*) \end{aligned} \right\} \quad (775)$$

Example 59. $N = 270$, $x = 22$, $100 p_x = 8.15$. $N = 270$ lies between $N_1 = 250$ and $N_2 = 300$. The interpolated limits for $100 p_x = 8.15$ in accordance with (774) are in column

$$\left\{ \begin{array}{ccc} N_2 = 300 & 100 p_1^{**} = 5.32 & 100 p_2^{**} = 11.86 \\ & 100 p_1^* = 5.00 & 100 p_2^* = 12.78 \end{array} \right.$$

$$\frac{V - N_1}{N_1 - N_1} = \frac{20}{50} = 0.4$$

$$100 p_1 = 5.08 + (0.4 \times 0.24) = 5.18 = \underline{5.2}$$

$$100 p_2 = 12.28 - (0.4 \times 0.42) = 12.11 = \underline{12.1}$$

(i) N lies above 1000. For $100 p_2$ ($= 100 x/N$) the limits $100 p_1'$ and $100 p_2'$ are looked for in the column $N = 1000$. Then

$$\left. \begin{aligned} 100 p_2 - 100 p_1' &= A \\ 100 p_2' - 100 p_2 &= B \\ 100 p_1 &= 100 p_2 - A \sqrt{1000/N} \\ 100 p_2 &= 100 p_2 + B \sqrt{1000/N} \end{aligned} \right\} (774)$$

Example 60. Given are $N = 3000$ and $x = 69$, $100 p_2 = 2.30$. For $100 p_2 = 2.30$, column $N = 1000$ gives the limits $100 p_1' = 1.46$ and $100 p_2' = 3.44$

$$A = 2.30 - 1.46 = 0.84$$

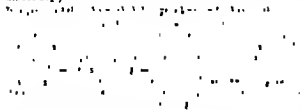
$$B = 3.44 - 2.30 = 1.14$$

$$\sqrt{1000/3000} = \sqrt{1/3} \approx 0.577$$

$$100 p_1 = 2.3 - (0.84 \times 0.577) = 1.82 = \underline{1.8}$$

$$100 p_2 = 2.3 + (1.14 \times 0.577) = 2.96 = \underline{3.0}$$

(ii) Significance limits for x , tables on pages 104–106 (or confidence limits for Np)



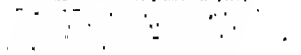
Example 61. Required are the 95% confidence limits for x for a sample of size $N = 10$ and a given $p = 0.5$

As shown by Figure 45, right, the lower limit x_1 is fixed so that confidence interval for p whose upper limit p_2 is closest to the given p without exceeding it (a) the upper limit x_2 is fixed by that confidence interval (b) whose lower limit p_1 lies closest to the given p without falling below it

In the table on page 85, $p_2 = 44/50$ is in accordance with (774a) and $p_1 = 55/50$ in accordance with (774b). The required limits for x are therefore $x_1 = 5$ and $x_2 = 5$.

According to WILKS²¹, the above significance limits correspond to the distribution-free confidence limits for quantiles $Q(p)$ (cf. section 01, page 161) when x_1 is replaced by $x_1 + 1$ and when p in the table is so chosen that it is of the same magnitude as p in $Q(p)$.

In this connection it should be noted [cf. (383)] that the postulated significance probability is reached when x attains or exceeds in an outward direction from Np the limits x_1 or x_2 .



one-tailed test) the sample originates from a population with $p > 0.05$ ($2\alpha = 0.025$)

two-tailed test) the sample originates from a population with $p \neq 0.05$ ($2\alpha = 0.05$)

On the basis of (780) and (782) or of (764) and (766) the following approximations are suitable for calculating the significance limits for x

$$x_1, x_2 = Np \pm (z_{\alpha} + z_{\beta}) \sqrt{Npq} \quad (778)$$

(cf. page 29, left hand table)

or, if $p < q$

$$\left. \begin{aligned} x_1 + 1, x_2 &= p \left(N + 1 - \frac{c^2}{4} \right) + \\ &+ \frac{c^2}{4} q \pm c \sqrt{pq \left(N + 1 - \frac{c^2}{4} \right)} \end{aligned} \right\} (779)$$

(cf. page 29, left hand table)

(c) Distribution-free tolerance limits for continuous distributions, table on page 128 (cf. also sections 8C, page 155, and 10F, page 161)

The values of the sample sizes N in this table have been calculated by an iterative process based on a formula of WILKS²¹, so that

$$\sum_{x=x_1}^{x_2} \binom{N}{x} \beta_p^x (1 - \beta_p)^{N-x} \approx 1 - \beta_c \quad (780)$$

The rounded-off values are based on the approximations²²

$$\left. \begin{aligned} N &\sim 1.03 x^2 + 4.74 x^3 - 1 \quad \text{for } \beta_p = 0.90 \\ N &\sim 1.01 x^2 + 9.75 x^3 - 1 \quad \text{for } \beta_p = 0.95 \\ N &\sim 1.00 x^2 + 49.75 x^3 - 1 \quad \text{for } \beta_p = 0.99 \end{aligned} \right\} (781)$$

where x^* is so chosen that $1/x^*$ of the table on pages 36–39 equals $1 - \beta_c$ for $v = 4x$.

The approximation to N obtained from (781) is very close to (780).

20G. Binomial distribution: Miscellaneous

(a) Arc-sine transformation, table on page 69 (cf. also 'Inverse trigonometric functions', page 139)

According to FREEMAN and TUKEY²³, the best transformation $x \rightarrow X$ for stabilizing the variance of the binomial distribution when $Np \geq 1$ is in most cases

$$X = \arcsin \sqrt{\frac{x}{N+1}} + \arcsin \sqrt{\frac{x+1}{N+1}} \quad (782)$$

with a variance within $\pm 6\%$ of

$$V_X = \frac{1}{N + \frac{1}{2}} \left(\text{angle in radians} \right)^2 \text{ or } \frac{821}{N + \frac{1}{2}} \left(\text{angle in degrees} \right)^2$$

The mean \bar{X} of the values thus transformed is approximately $2 \arcsin \sqrt{p}$

This transformation can be used in variance analysis and other operations

(b) With a given p , how large must the sample size N be for the event E to occur at least x times with a probability p^* ? The solution of this problem for $x = 1$ is given in (755)

The simplest approximate solution for $x > 1$, on the basis of (764), is (when $p < q$)

$$N \sim \frac{1}{p} \left(\frac{c^2}{4} + x + \epsilon \sqrt{xq} \right) - 1 \quad (783)$$

where $\epsilon = \pm 1$.

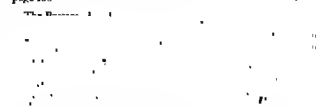
21. The Poisson distribution

21A. General

E is a random event occurring over a long period of observation²⁴ an infinite number of times but in a relatively short time²⁵ (in general the observation unit t) only rarely. The probability that in an observation unit t the event will occur 0, 1, 2, ..., x times is then

$$f(x) = P_x = \frac{e^{-\lambda} \lambda^x}{x!} = \frac{e^{-\lambda} \lambda^1}{0!} + \frac{e^{-\lambda} \lambda^2}{1!} + \frac{e^{-\lambda} \lambda^3}{2!} + \dots \quad (784)$$

e = base of natural logarithms, t = observation unit; for λ see (787), page 188



The simplest calculation of several successive individual probabilities is from the recursion formula

$$P_{x+1} = P_x \times \frac{\lambda}{x+1} \quad (785)$$

²⁴ Time has been chosen as an example. The same argument would apply, for instance, to surfaces and volumes.

Example 63. For the Poisson distribution ($\lambda = 1$) calculate the individual probabilities for x from 0 to 5.

$$\begin{aligned} P_0 &= 1/e = 0.367879 & P_2 &= P_1 \times 1/2 = 0.061313 \\ P_1 &= P_0 \times 1 = 0.367879 & P_3 &= P_2 \times 1/3 = 0.015328 \\ P_2 &= P_1 \times 1/2 = 0.183940 & P_4 &= P_3 \times 1/4 = 0.003066 \end{aligned}$$

Calculation of the *cumulative probabilities* is carried out according to the procedure given in section 5, page 148, with N replaced by infinity. It should also be noted that in the Poisson distribution the probability $\text{Prob}(x \geq k)$ can be calculated only from the probability $\text{Prob}(x \leq k-1)$, i.e.,

$$\text{Prob}(x \geq k) = 1 - \text{Prob}(x \leq k-1)$$

Example 64. How large must λ be for the event E to occur at least once during the observation unit t with a probability p^* ? This is an unusual problem in the Poisson distribution but sometimes occurs when the latter is used as an approximation to other distributions.)

The solution is obtained by using equation (129) on page 137. Let the numerical values for various probabilities p^* can also be found. For $p^* = 0.999$, λ for example is 6.9.

B. The addition theorem for the Poisson distribution

x_1, x_2, \dots, x_k are stochastically independent† random variables with Poisson distributions $(\lambda_1), (\lambda_2), \dots, (\lambda_k)$ respectively, then their sum $x = x_1 + x_2 + \dots + x_k$ is likewise a Poisson distribution (λ) with $\lambda = \lambda_1 + \lambda_2 + \dots + \lambda_k$. (786)

C. Parameters and their estimates

The mean of the Poisson distribution is

$$\begin{aligned} \mu_{x_i} &= \lambda_i = \text{expectation of } x_i & (a) \\ \text{and the variance} & & \\ \sigma_{x_i}^2 &= \lambda_i = \text{expectation of } x_i & (b) \end{aligned} \quad (787)$$

where i = observation unit to which x and λ_i relate.

If a Poisson distribution with observation unit i is used to calculate another Poisson distribution with observation unit k , then the mean and variance of the latter are

$$\mu_{x_{ki}}, \sigma_{x_{ki}}^2 = k\lambda_i; (k > 0) \quad (788)$$

The equal magnitude of mean and variance in the Poisson distribution results in the following rule of thumb:

The ratio of mean to variance in a discrete distribution is approximately unity (say between $1/10$ and $1/10$), then a Poisson distribution is likely to approximate to it provided that variable x can assume high (theoretically, infinitely high) values. (789)

Unbiased estimates of λ_i based on n equal observation units i are

$$\begin{aligned} \bar{x}_i &= \frac{\sum x_i}{n} = \frac{\sum x_i f_i}{n} & (a) \\ \hat{x}_i &= \frac{\sum x_i^2 - (\sum x_i)^2/n}{n-1} = \frac{\sum x_i^2 f_i - (\sum x_i f_i)^2/n}{n-1} = \frac{S_i}{n-1} & (b) \end{aligned} \quad (790)$$

\bar{x}_i is the *better* (more efficient) estimate. Since it is also more easily calculated it is the one usually used. With higher values of n ($n > 5$), however, the additional calculation of $(n-1)^{-1}$ [the numerator in (790b)] offers the advantage of being able to test whether ratio \hat{x}_i/\bar{x}_i differs significantly from 1. The test quotient is

$$\frac{(n-1)\hat{x}_i^2}{\bar{x}_i^2} = \frac{S_i}{\bar{x}_i^2} \quad (791)$$

significance limit χ^2 with $\nu = n-1$, $2\alpha = 1\%$, pages 36-39

If the test quotient (791) attains or exceeds the significance limit, the sample probably does not originate from a Poisson distribution. This leads to the following rule of thumb:

If (791) is significant, the sample could originate from a binomial distribution when $\hat{x}_i < \bar{x}_i$ from a binomial distribution with negative index when $\hat{x}_i > \bar{x}_i$. Cf. also Bliss α^2 . (792)

Example 65. In 60 minutes 12 events are observed. $\lambda_{12/1} = 12$. In accordance with (788), the estimate of $\lambda_{1 \text{ min}}$ $12/60 = 1/5$.

Example 66. In 60 minutes 12 events are observed, in 30 minutes 8. In accordance with (786), $\lambda_{90 \text{ min}} = 12 + 8 = 20$, $\lambda_{1 \text{ min}} = 20/60 = 1/3$.

Example 67. In 100 observation periods of 1 minute each event E is observed x_i times in f_i observation periods, as follows:

x_i	f_i	$x_i f_i$	$x_i^2 f_i$	
0	5	0	0	
1	30	30	30	$\bar{x}_i = 2.36$ from (790)
2	24	48	96	
3	20	60	180	$S_i = 778 - 556.96$
4	12	48	192	$= 221.04$ from (791)
5	4	20	100	
6	5	30	180	$\chi^2 = 93.661$,
7	0			$\nu = 99$ from (791)
8	0			
$n = 100 \quad \Sigma x = 236 \quad \Sigma x^2 = 778$				
$= \lambda_{100 \text{ min}}$				

In this case χ^2 lies far inside the significance limit of 0.05 ($\alpha < 0.35$), so that the distribution *could* be a Poisson distribution. A more efficient test is provided by calculation of the *fitted* Poisson distribution in accordance with (784) with $\lambda = 2.36$, multiplied of the value obtained by n and then testing with χ^2 in accordance with (566) with degrees of freedom $\nu = k - 2$ from (569a), k = number of classes i .

21D. Transformations

As shown by Figure 44 (page 185), with increasing λ the shape of the Poisson distribution gradually (and fairly rapidly) approaches that of the normal distribution.

$$\frac{e^{-\lambda} \lambda^x}{x!} \rightarrow \frac{1}{\sqrt{2\pi\lambda}} e^{-\frac{(x-\lambda)^2}{2\lambda}}$$

as $\lambda \rightarrow \infty$.

The corresponding transformations are analogous to the transformations of the binomial distribution to the normal distribution using (760)-(763), with Np replaced by λ .

The following approximations are better²⁹:

$$\begin{aligned} c_p &= 2(\sqrt{\lambda_p + 1} - \sqrt{\lambda}) \\ x_p &= \lambda + c_p \sqrt{\lambda} + \frac{c_p^2}{4} - 1 \\ c_{1-p} &= 2(\sqrt{\lambda_{1-p}} - \sqrt{\lambda}) \\ x_{1-p} &= \lambda + c_{1-p} \sqrt{\lambda} + \frac{c_{1-p}^2}{4} \end{aligned} \quad \left. \begin{array}{l} \\ \\ \\ \end{array} \right\} \lambda \geq 1$$

Example 68. Calculate x_p and x_{1-p} for $p = p^* = 0.025$ of Poisson distribution ($\lambda = 99$).

$$x_p = 99 - 1.96 \sqrt{99} + \frac{1.96^2}{4} - 1 = 79.46 \text{ from (795)}$$

$$x_{1-p} = 99 + 1.96 \sqrt{99} + \frac{1.96^2}{4} = 119.46 \text{ from (797)}$$

Since x can have only discrete values, these results are rounded off to give 79 and 119. The exact values are 79 and 120. In this connection it should be noted that in such cases it is better to be on the safe side and round off outwards:

In order more adequately to meet the requirements $\text{Prob}(x \leq x_p) \leq p$ and $\text{Prob}(x \geq x_{1-p}) \leq p^*$, x_p should always be rounded off downwards, x_{1-p} always upwards. This also applies to approximations to other discrete distributions. (793)

If rule (793) had been adhered to in example 68, the correct result would have been obtained. However, this is not necessarily always the case when (798) is adhered to.

The following transformation¹⁰ is suitable for stabilizing the variance

$$X' = \sqrt{X} + \sqrt{X+1}$$

with variance $\sigma_{X'}^2 \sim 1$

and mean $X' \sim \sqrt{4\lambda + 1}$

(799)

The relationship between the Poisson and χ^2 distributions is given in (341) and (342), whence the following procedure for determining the exact values of x_p and x_{p^*} :

(a) x_p is required. The value $\chi^2 \leq 2\lambda$ is looked for in the column $1/f_1 = 1 - p$ of the χ^2 table on pages 36-39. From the degrees of freedom v of this χ^2 it follows that

$$x_p = \frac{v}{2} - 1 \text{ when } v \text{ is even}$$

$$= \frac{v}{2} - 1.5 \text{ when } v \text{ is odd}$$

(800)

(b) x_{p^*} is required. The value $\chi^2 \geq 2\lambda$ is looked for in the column $1/f_1 = p^*$ of the χ^2 table on pages 36-39. From the degrees of freedom v of this χ^2 it follows that

$$x_{p^*} = \frac{v}{2} \text{ when } v \text{ is even}$$

$$= \frac{v}{2} + 0.5 \text{ when } v \text{ is odd}$$

(801)

Example 69 Required are the $(1 - 2\alpha)$ limits for x when $\lambda = 32$ and $\alpha = 0.005$. The left limit is obtained from (800) and is $x_{1-2\alpha}^* = 63.582 \approx 64$ with $v = 31$. $x_1 = 31/2 - 1.5 = 14$. The right limit is obtained from (801) and is $x_{1-2\alpha} = 64.526 \approx 64$ with $v = 106$. $x_1 = 106/2 = 53$.

21F. Confidence limits and significance limits

(a) *Confidence limits for λ* (tables on pages 107 and 108)

In analogy with the binomial distribution, confidence limits for λ are solutions of the equations

$$\sum_{k=0}^{x_1} \frac{e^{-\lambda} \lambda^k}{k!} = \alpha \text{ and } \sum_{k=x_2}^{\infty} \frac{e^{-\lambda} \lambda^k}{k!} = \alpha, \alpha < 0.5 \quad (a) \quad (b) \quad (802)$$

for λ_1 and λ_2 .

For $x = 0$ there is only one $(1 - \alpha)$ confidence interval with the solution $\lambda = x$ (equation (129), page 137). The left limit λ_1 is zero.

For $x > 0$ only iterative solutions are possible. The tables on pages 107 and 108 were calculated in this way by computer for values of λ up to 100. For values of $x > 100$ the formulae (804) were used (from FREEMAN and TUCKER's approximation²⁹).

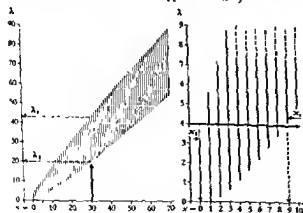


Fig. 46. Poisson distribution, confidence limits for λ .

For significance probabilities other than those in the tables on pages 107 and 108, exact limits for x up to 100 (or 99) can be calculated from the χ^2 table on pages 36-39 as follows:

Given x and α , then

$$x_1 [x_1 - 1, \dots, 1] = \lambda_1$$

$$x_2 [x_2 - 1, \dots, 1, 0] = \lambda_2$$

(a)

(b)

where x_1^* and x_2^* denote the α and $1 - \alpha$ quantiles, α are to be found under $1/f_1$.

Example 70. Required are the $(1 - 2\alpha)$ limits for λ when $\alpha = 0.05$. For λ_1 the table is entered at $v = 2 \times 98 = 196$, $1 - 0.05$, giving $\chi^2 = 164.10$. $\lambda_1 = 164.10/2 = 82.05$. For λ_2 the table is entered at $v = 2(98 + 1) = 198$ and $1/f_1 = 0.9$ giving $\chi^2 = 231.829$. $\lambda_2 = 231.829/2 = 115.915$.

For higher values of α , very good approximations are from (794) and (794):

$$\lambda_1, \lambda_2 = \left(\frac{1 - \alpha}{2} \mp \sqrt{x + \frac{1}{2} \mp \frac{1}{2}} \right)^2$$

Example 71. Required are the $(1 - 2\alpha)$ confidence limits for $x = 99$ and $\alpha = 0.025$.

$$\lambda_1 = \left(\frac{1.96}{2} - \sqrt{99 + \frac{1}{2} - \frac{1}{2}} \right)^2 = 80.459$$

$$\lambda_2 = \left(\frac{1.96}{2} + \sqrt{99 + \frac{1}{2} + \frac{1}{2}} \right)^2 = 120.56$$

The exact values are 80.458 and 120.53.

Example 72 In 12 minutes 24 events are observed. Calculate 95% limits for $\lambda_{12 \text{ min}}$, $\lambda_{1 \text{ min}}$, $\lambda_{1 \text{ hr}}$. For $v = 24$ in the table of the limits 15.378 and 35.711 are given. In accordance with these give the following further limits

$$\text{for } \lambda_{12 \text{ min}} = 15.378/12 \text{ and } 35.711/12 = 1.2815 \text{ and } 2.9759$$

$$\text{for } \lambda_{1 \text{ min}} = 15.378 \times 5 \text{ and } 35.711 \times 5 = 76.890 \text{ and } 178.555$$

The estimate of the limits for $\lambda_{1 \text{ hr}}$ must always be based on the basis of the number of events x observed during the interval t , and not on the basis of this number multiplied. The following calculation in the case of example 72 would be

$$x_{12 \text{ min}} = 24/12 = 2, \text{ limits } 0.2422 - 2.7247$$

$$\text{or } x_{1 \text{ min}} = 24 \times 5 = 120, \text{ limits } 99.49 - 143.52$$

(b) *Significance limits for x when λ is given* (table on page 109)

These limits meet the condition (790) with N replaced by x . They can be obtained without calculation from the t limits for λ , as shown in Figure 46, right. The procedure analogous to that for determining the corresponding limits for the binomial distribution. For $\alpha \neq 0.025$ or 0.005 , the left limit (from (800)), the right limit from (801). Cf. example page. For $n > 100$ (or 99), approximations are obtained. and (797).

22. The hypergeometric distribution

22A. General

Given are N balls, of which X are white and $N - X$ are black. The probability of drawing exactly x_1 white balls in N_1 draws

$$f(x_1 | X, N, N_1) = \frac{\binom{X}{x_1} \binom{N-X}{N_1-x_1}}{\binom{N}{N_1}} = \frac{N! (N-X)!}{N_1! (N-N_1)!} \frac{X! (N-X)!}{x_1! (N-x_1)!} \quad (803)$$

$f(x_1 | X, N, N_1)$ is known as the hypergeometric distribution (X, N, N_1 constant).

The corresponding fourfold table (cf. section 22D, p. 100)

White x_1	$N_1 - x_1$	N_1	$x_1 N_1 - x_1^2$
Red $X - x_1$	$N - X - N_1 + x_1$	$N - N_1$	$(X - x_1)(N - N_1 + x_1)$
X	$N - X$	N	$X(N - X)$

For $N \leq 100$ the calculation of (803) is best made from the tables on pages 70-77 (cf. explanation on p. 70). For $N > 100$ from (b) by means of the tables on pages 26 a calculation can also be made with the aid of the recursion

$$f(x_1 + 1 | X) = [f(x_1 | X)] \times \frac{(N_1 - x_1)(X - x_1)}{(x_1 + 1)(N - X - N_1 + x_1)}$$

and

$$f(x_1 - 1 | X) = [f(x_1 | X)] \times \frac{(N - X - N_1 + x_1)(X + x_1)}{(N - X)(X + 1 - x_1)}$$

Hypergeometric distribution, $N = 20$, $N_1 = 5$, individual probabilities $\text{Prob}(x_1 = k_1 | X = K)$

N_1	$X = K$																			
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
0	1	0.75	0.5526	0.3991	0.2817	0.1937	0.1291	0.0830	0.0511	0.0298	0.0163	0.0081	0.0036	0.0014	0.0004	0.0001				
1		0.25	0.3947	0.4605	0.4696	0.4402	0.3874	0.3228	0.2554	0.1916	0.1354	0.0894	0.0542	0.0293	0.0135	0.0048	0.0010			
2			0.0526	0.1316	0.2167	0.2935	0.3522	0.3874	0.3973	0.3831	0.3483	0.2980	0.2384	0.1761	0.1174	0.0677	0.0310	0.0088		
3				0.0088	0.0310	0.0677	0.1174	0.1761	0.2384	0.2980	0.3483	0.3831	0.3973	0.3874	0.3522	0.2935	0.2167	0.1316	0.0526	
4					0.0010	0.0048	0.0135	0.0293	0.0542	0.0894	0.1354	0.1916	0.2554	0.3228	0.3874	0.4402	0.4696	0.4605	0.3947	0.25
5						0.0001	0.0004	0.0014	0.0036	0.0081	0.0163	0.0298	0.0511	0.0830	0.1291	0.1937	0.2817	0.3991	0.5526	0.75

Hypergeometric distribution, $N = 20$, $N_1 = 5$, cumulative probabilities $\text{Prob}(x_1 \leq k_1 | X = K)$

N_1	$X = K$																			
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
0	1	0.75	0.5526	0.3991	0.2817	0.1937	0.1291	0.0830	0.0511	0.0298	0.0163	0.0081	0.0036	0.0011	0.0004	0.0001				
1		1	0.9474	0.8596	0.7513	0.6339	0.5165	0.4058	0.3065	0.2214	0.1517	0.0975	0.0578	0.0307	0.0139	0.0049	0.0010			
2			1	0.9912	0.9680	0.9274	0.8687	0.7932	0.7038	0.6045	0.5000	0.3955	0.2962	0.2068	0.1313	0.0726	0.0320	0.0088		
3				1	0.9990	0.9951	0.9861	0.9693	0.9422	0.9025	0.8483	0.7786	0.6935	0.5942	0.4835	0.3661	0.2487	0.1404	0.0526	
4					1	0.9999	0.9996	0.9986	0.9964	0.9919	0.9837	0.9702	0.9489	0.9170	0.8709	0.8063	0.7183	0.6009	0.4474	0.25
5						1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

$\text{Prob}(x_1 = k_1 | X = K; N = 20, N_1 = 5)$

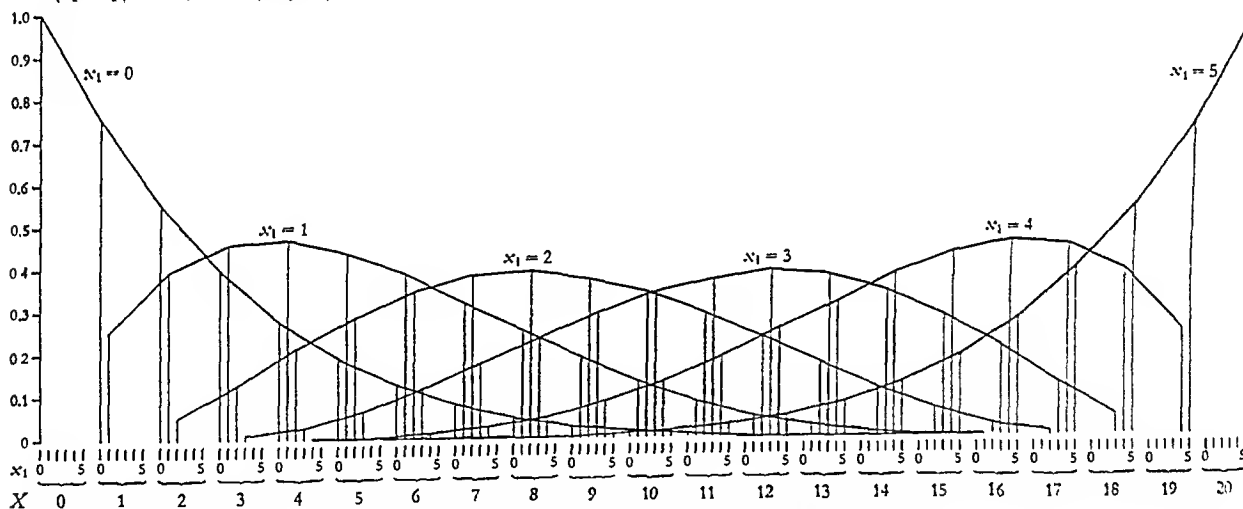


Fig. 47. Hypergeometric distribution. Graphical representation of all possible individual probabilities when N and N_1 are given. The vertical strokes 0-5 represent the probabilities $\text{Prob}(x_1 = 0, 1, \dots, 5 | X = K)$. The curves link the probabilities $\text{Prob}(x_1 = k_1 | X = 0, 1, \dots, 20)$.

$\text{Prob}(x_1 \leq k_1 | X = K; N = 20, N_1 = 5)$

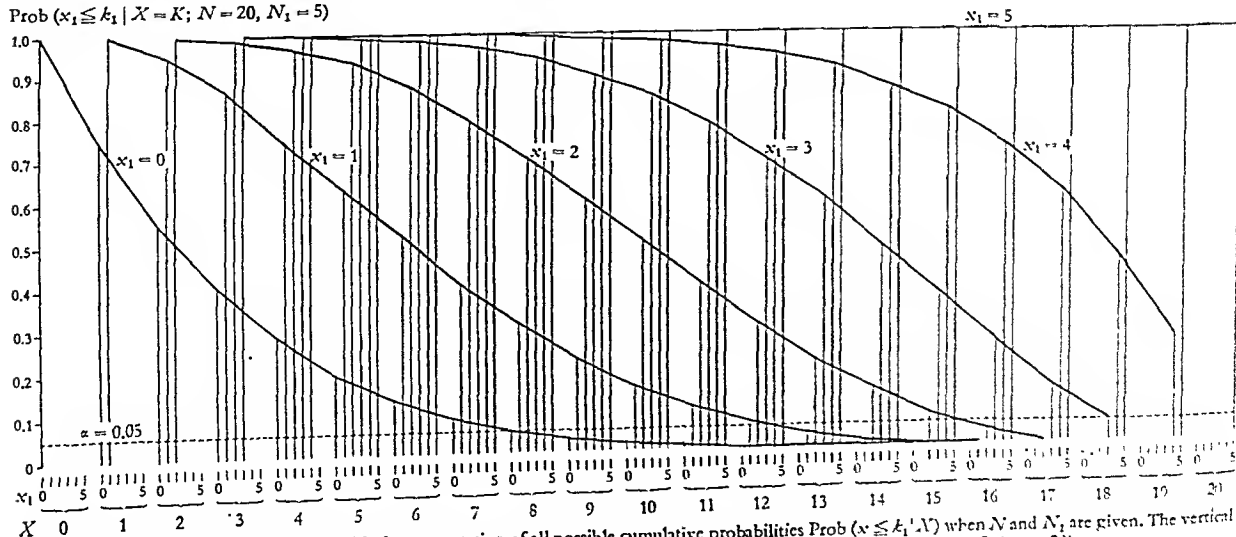


Fig. 48. Hypergeometric distribution. Graphical representation of all possible cumulative probabilities $\text{Prob}(x \leq k_1 | X)$ when N and N_1 are given. The vertical strokes 0-5 represent the probabilities $\text{Prob}(x_1 \leq 0, 1, \dots, 5 | X = K)$. The curves link the probabilities $\text{Prob}(x \leq k_1 | X = 0, 1, \dots, 20)$.

All the probabilities $f(x_i | X, N, N_1 = 5)$ and cumulative probabilities $F(x_i | X)$ are given in the tables on page 190, where the same probabilities are shown graphically in Figures 47 and 48

A check on calculations of this kind is provided by

$$\left. \begin{aligned} \sum_{x_1=0}^{x=N} \text{Prob}(x_1 | X=N) &= 1 \\ \sum_{x_1=N-N_1+1}^{x=N} \text{Prob}(x_1 = k_1 | X) &= \frac{N+1}{N_1+1} \end{aligned} \right\} \quad (809)$$

Figure 47 clearly demonstrates the symmetry of the relationship

$$\left. \begin{aligned} \text{Prob}(x_1 = k_1 | X=N) &= \text{Prob}(x_1 = N_1 - k_1 | X=N-N) \\ \text{hence} \\ \text{Prob}(x_1 \leq k_1 | X=N) &= \text{Prob}(x_1 \geq N_1 - k_1 | X=N-N) \end{aligned} \right\} \quad (810)$$

2B. Parameters

The mean of x when X, N and N_1 are given is (putting $X/N = p$)

$$\mu_x = N_1 p \quad (811)$$

and the variance is

$$\sigma_x^2 = N_1 p q \left(\frac{N-N_1}{N-1} \right) \left\{ \begin{aligned} X/N &= p, \\ q &= 1-p \end{aligned} \right. \quad (812)$$

The variance of the hypergeometric distribution (N, N_1, p) is *smaller* than that of the binomial distribution (p, N_1) by the factor $(N-N_1)/(N-1)$

2C. The hypergeometric distribution and other distributions

$$\left. \begin{aligned} \text{When } N_1/N < 0.1 \text{ and } N \text{ is fairly large the Poisson distribution } (\lambda = N_1 p) \text{ is a good approximation} \\ \text{When } N_1 p \geq 4 \text{ (about), the normal distribution [(811), (812)] is a good approximation, whence} \end{aligned} \right\} \quad (813)$$

$$\left. \begin{aligned} c_p = \frac{x_1 + \frac{1}{2} - (811)}{\sqrt{(812)}} \\ c_{1-p} = \frac{x_1 - \frac{1}{2} - (811)}{\sqrt{(812)}} \end{aligned} \right\} \quad (814)$$

$$\left. \begin{aligned} \text{where } +\frac{1}{2} \text{ or } -\frac{1}{2} \text{ can be neglected when } N \text{ is large} \end{aligned} \right\} \quad (815)$$

$$\left. \begin{aligned} \text{For } m = 2 \text{ (2 samples)} \\ \text{one-tailed test } \left\{ \begin{aligned} p_1 < p_2, \text{ if } p_1 - p_2 < 0 \text{ (a)} \\ p_1 > p_2, \text{ if } p_1 - p_2 > 0 \text{ (b)} \end{aligned} \right. \\ \text{two-tailed test } p_1 \neq p_2 \text{ (2a)} \end{aligned} \right\} \quad (821)$$

where $+ \frac{1}{2}$ or $- \frac{1}{2}$ can be neglected when N is large

22D. Significance limits (fourfold table test)

(Cf. remarks on page 123)

The significance limits given in the table on pages 109-123 meet the conditions (when N and N_1 are given)

$$\left. \begin{aligned} \text{Prob}(x_1 \geq k_1 | X) \leq \alpha \\ \text{Prob}(x_1 \geq k_1 | X+1) > \alpha \end{aligned} \right\} \quad (a) \quad (817)$$

and

$$\left. \begin{aligned} \text{Prob}(x_1 \leq k_1 | X) \leq \alpha \\ \text{Prob}(x_1 \leq k_1 | X-1) > \alpha \end{aligned} \right\} \quad (b)$$

This form of presentation is preferred since it is also convenient in situations in which X is unknown (these do not correspond to the situation described at the start of section 22A, page 189)

The procedure for finding the upper level (817b) for $\alpha = 0.05$ is indicated in Figure 48 (horizontal broken line)

With large values of N_1 (817) can be satisfied approximately on the basis of (814) as follows:

$$\left. \begin{aligned} X_1, X_2 = \frac{N}{2k} \left(k + 2x_1 - N_1 - 1 \mp \sqrt{k^2 - \frac{2k}{N_1} [(x_1 \mp \frac{1}{2})^2 + (N_1 - x_1 \pm \frac{1}{2})^2] + (2x_1 - N_1 \mp 1)^2} \right) \end{aligned} \right\} \quad (818)$$

or without continuity correction

$$\left. \begin{aligned} X_1, X_2 = \frac{N}{2k} \left(k + 2x_1 - N_1 \mp \sqrt{k^2 - \frac{2k}{N_1} [x_1^2 + (N_1 - x_1)^2] + (2x_1 - N_1)^2} \right) \end{aligned} \right\} \quad (b)$$

where in (a) and (b) $k = N_1 + (1 - N_1/N)x_1^2 - x_2^2$ for $v = 1, 2, \alpha = 1 - \beta$, page 36

When $N > 60, N_1 p \geq 4, N_1 q \geq 4$ (about), the $(1 - 2\alpha)$ significance limits for x_1 with X given can be obtained approximately as follows:

$$x_{1a}, x_{1b} = N_1 p \mp \left[\frac{1}{2} + t_{\alpha} \sqrt{N_1 p q (N - N_1) / (N - 1)} \right] \quad (819)$$

For p and q see (811)

23. Testing frequencies

23A. Samples from binomially distributed populations

$$\left. \begin{aligned} \text{Given } m \text{ samples of sizes } N_1, N_2, \dots, N_m \text{ in which the event } E \text{ occurs } x_1, x_2, \dots, x_m \text{ times respectively, the following are calculated:} \end{aligned} \right\} \quad (820)$$

(b) Given several (m) samples of sizes N_1, N_2, \dots, N_m in which the event E occurs x_1, x_2, \dots, x_m times respectively, the following are calculated:

$$p_i = \frac{x_i}{N_i}, \quad q_i = 1 - p_i, \quad \bar{p} = (\sum x_i) / (\sum N_i), \quad \bar{q} = 1 - \bar{p}$$

The x_i values are now transformed as follows in accordance with (744) and (746)

$$\left. \begin{aligned} c_i = 2 \left\{ \sqrt{(x_i + 1) \bar{q}} - \sqrt{(N_i - x_i) \bar{p}} \right\}, \text{ when } p_i < \bar{p} \\ \text{or} \\ c_i = 2 \left\{ \sqrt{x_i \bar{q}} - \sqrt{(N_i - x_i + 1) \bar{p}} \right\}, \text{ when } p_i > \bar{p} \end{aligned} \right\} \quad (821)$$

A comparison of the transformed data can be made by two methods

I Comparison on the basis of the extreme range (rapid test)

The difference between the highest and lowest values of c_i is the extreme range m, c_1 being obtained from (821)

$$\left. \begin{aligned} \text{For } m = 2 \text{ (2 samples)} \\ \text{one-tailed test } \left\{ \begin{aligned} p_1 < p_2, \text{ if } p_1 - p_2 < 0 \text{ (a)} \\ p_1 > p_2, \text{ if } p_1 - p_2 > 0 \text{ (b)} \end{aligned} \right. \\ \text{two-tailed test } p_1 \neq p_2 \text{ (2a)} \end{aligned} \right\} \quad (822)$$

For $m = 2$ (2 samples)

$$\left. \begin{aligned} \text{one-tailed test } \left\{ \begin{aligned} p_1 < p_2, \text{ if } p_1 - p_2 < 0 \text{ (a)} \\ p_1 > p_2, \text{ if } p_1 - p_2 > 0 \text{ (b)} \end{aligned} \right. \\ \text{two-tailed test } p_1 \neq p_2 \text{ (2a)} \end{aligned} \right\} \quad (823)$$

For $m > 2$ (more than 2 samples)

two-tailed test: the samples do not all originate from the same population

When $m = 2$ (2 samples), this test has the same power as the following χ^2 test. The range test is *not* recommended when $m > 10$.

II Comparison on the basis of χ^2

The squares of the c_i values are summed. Then the significance limit for the test statistic

$$\left. \begin{aligned} \sum c_i^2 \\ \text{is found from } \chi^2, \text{ pages 36-39, with degrees of freedom } v = m - 1 \text{ (cf. section 12B, page 166)} \end{aligned} \right\} \quad (825)$$

23B. Samples from multinomially distributed populations

Given are m samples of sizes $N_1, N_2, \dots, N_t, \dots, N_m$, in which the events $E_1, E_2, \dots, E_j, \dots, E_n$ occur $x_{1j}, x_{2j}, \dots, x_{tj}, \dots, x_{mj}$ times respectively, and

$$\left. \begin{array}{l} \sum_{j=1}^n x_{1j} = N_1, \sum_{j=1}^n x_{2j} = N_2, \dots, \sum_{j=1}^n x_{tj} = N_t, \dots, \sum_{j=1}^n x_{mj} = N_m \\ \begin{array}{cccc|c} x_{11} & x_{12} & \dots & x_{1j} & \dots & x_{1n} & N_1 \\ x_{21} & x_{22} & \dots & x_{2j} & \dots & x_{2n} & N_2 \\ \vdots & \vdots & & \vdots & & \vdots & \vdots \\ x_{t1} & x_{t2} & \dots & x_{tj} & \dots & x_{tn} & N_t \\ \vdots & \vdots & & \vdots & & \vdots & \vdots \\ x_{m1} & x_{m2} & \dots & x_{mj} & \dots & x_{mn} & N_m \\ \hline X_1 & X_2 & \dots & X_j & \dots & X_n & N \end{array} \end{array} \right\} \quad (826)$$

The expected values $E_{ij} = N_i X_j / N$ on the assumption of constant probabilities and independence are now calculated. The expected value of x_{11} (event 1 in sample 1), for example, is $N_1 X_1 / N$. With these expected values the following quotient is calculated for each observation x_{ij} :

$$\frac{(x_{ij} - E_{ij})^2}{E_{ij}} \quad \text{or} \quad \frac{x_{ij}^2}{X_j N_i} - 1 \quad (a) \quad (b) \quad (827)$$

and the values summed. The significance limit for the sum

$$\sum_{i=1}^m \sum_{j=1}^n (827a) \quad \text{or} \quad N \sum_{i=1}^m \sum_{j=1}^n (827b) \quad (828)$$

is found from χ^2 , pages 36–39, with degrees of freedom $v = (n - 1)(m - 1)$ and $2\alpha = 1\%$. If the test statistic (828) attains or exceeds the significance limit, then interpretation (825) is valid.

23C. Samples from Poisson distributions

(a) 2 samples from two observation units of equal magnitude $t_1 = t_2 = t$

Given are 2 samples with the same observation unit $t_1 = t_2 = t$, in which the event E occurs x_1 and x_2 times respectively.

The sums $x_1 + x_2 = N$ are calculated. The significance limits for x_1 and x_2 are then x_t and x_r of the table on pages 105 and 106 for $N = x_1 + x_2$. If x_1 and x_2 attain or exceed these limits (in an outward direction from $\frac{1}{2}N$), then the following interpretations may be made:

$$\left. \begin{array}{l} \text{one-tailed test: } \begin{cases} \lambda_1 < \lambda_2, \text{ if } x_1 \leq x_t \text{ (significance } \alpha) \\ \lambda_1 > \lambda_2, \text{ if } x_1 \geq x_r \text{ (significance } \alpha) \end{cases} \\ \text{two-tailed test: } \lambda_1 \neq \lambda_2, \text{ if } x_1 \text{ and } x_2 \text{ attain or exceed} \\ \text{(outwards) the levels } x_t \text{ and } x_r \\ \text{(significance } 2\alpha) \end{array} \right\} \quad (829)$$

For samples with $x_1 + x_2 > 1000$ or $t_1 \neq t_2$ see (b) below.

(b) Several samples from any number of observation units t_i

Given are m samples from any number of observation units $t_1, t_2, \dots, t_t, \dots, t_m$ in which the event E occurs $x_1, x_2, \dots, x_t, \dots, x_m$ times. The following are calculated:

$$\lambda_i^* = \frac{x_i}{t_i} \quad \text{and} \quad \bar{\lambda} = (\sum x_i) / (\sum t_i)$$

and the x_i values transformed into c_i values as follows in accordance with (794) and (796):

$$\left. \begin{array}{l} c_i = 2 \left(\sqrt{x_i + 1} - \sqrt{t_i \bar{\lambda}} \right), \text{ if } \lambda_i^* < \bar{\lambda} \\ c_i = 2 \left(\sqrt{x_i} - \sqrt{t_i \bar{\lambda}} \right), \text{ if } \lambda_i^* > \bar{\lambda} \end{array} \right\} \quad (830)$$

Comparison of these transformed data and their interpretations are as in section 23A (b), I and II, with $\bar{\lambda}$ and λ_i^* in place of \bar{p} and p_i .

(c) Confidence limits for the increase in frequency of a rare event³⁵

Given are two samples of sizes N_1 and N_2 in which the fairly rare event E occurs with a relative frequency of $p_1 = x_1/N_1$ and $p_2 = x_2/N_2$ respectively. The samples should be so numbered that $p_1 < p_2$. The estimate of the proportionate increase in relative frequency from sample 1 to sample 2 is then

$$Proc_{1 \rightarrow 2} = \frac{p_2 - p_1}{p_1} \quad (831)$$

with the $(1 - 2\alpha)$ confidence limits for $Proc_{1 \rightarrow 2}$

$$k \left(\frac{1}{p_r} - 1 \right) - 1 < Proc_{1 \rightarrow 2} < k \left(\frac{1}{p_t} - 1 \right) - 1 \quad (832)$$

where $k = N_1/N_2$ and p_r and p_t are obtained from the confidence limits for p of the binomial distribution on page 103 for $N = x_1 + x_2$ and $x = x_1$. (831) and (832) are converted percentages by multiplying by 100. (832) can also be calculated this way when only the ratio N_1/N_2 and the absolute number and x_2 are known. Interpretation: When the left limit of (832) is zero, then no increase in frequency has occurred.

24. Rank tests

24A. Ranking

(a) By magnitude (continuous distributions). Given are samples 1 and 2 with the x_1 values 1.06, 1.53, 1.68, 1.68, 1.69, and the x_2 values 1.30, 1.55, 1.69, 1.80. These values are ranked as follows:

$$\left. \begin{array}{cccccccccccc} x_1 & 1.06 & 1.53 & 1.68 & 1.68 & 1.69 & 1.69 & & & & & \\ x_2 & & 1.30 & 1.55 & & 1.69 & & & & & 1.80 & \\ O_{1,2} & 1 & 2 & 3 & 4 & 5 & 6 & 8 & 8 & 8 & 10 & \\ & & & & & & & \underbrace{8+8+9}_{=25} & & & & \end{array} \right\}$$

With ties [cf. (346)], the procedure is as in (833): tied values within a sample receive successive rank numbers, those between the samples the mean of the two rank numbers at the position concerned.

In the above example, the rank numbers O_i of the x_1 values are $O_1 = 1, 3, 5, 6, 8$ and 8, and their sum $T_1 = \sum O_i = 31$.

With paired observations, the n pair differences d_i are calculated as in section 16D, page 173, with all d_i values equal to zero ignored and N reduced accordingly. The absolute values of these differences are then ranked and either the rank numbers of all negative differences summed to give T_- or those of all positive differences summed to give T_+ .

(b) By order in a series (discrete distributions). If in a series of N trials the event E occurs once each in the 2nd, 3rd, 8th and 13th trials, in all N_i times (for example 4 times), then $O_E = 2, 3, 8$ and 13 respectively and the sum of the O_E numbers $= T_E = 26$.

24B. The Wilcoxon test for two samples^{36,37}

Given are two samples from continuous distributions of any form with means μ_1 and μ_2 respectively. These are so numbered that $N_1 \leq 25$ and $N_2 \leq 50$. The x_i values are now ranked as in (831) and (834) to give the sum T_1 of (835).

The significance limits for T_1 are given in the tables on pages 124–127. If T_1 attains the significance levels or exceeds them in the outward direction from its expected value, then this may be regarded as evidence that

$$\left. \begin{array}{l} \text{one-tailed test: } \begin{cases} \mu_1 < \mu_2, \text{ if } T_1 \leq T_l (\leq \alpha) \\ \mu_1 > \mu_2, \text{ if } T_1 \geq T_r (\leq \alpha) \end{cases} \\ \text{two-tailed test: } \mu_1 \neq \mu_2, \text{ if } T_1 \leq T_l \text{ or } T_1 \geq T_r (\leq 2\alpha) \end{array} \right\} \quad (83)$$

Cf. also section 9C, page 157.

Under the null hypothesis, the expectation T_1 of the estimator T_1 is

$$\left. \begin{array}{l} T_1 = N_1(N_1 + N_2 + 1)/2 \quad \text{or} \quad (a) \\ 6 T_1 = 3 N_1(N_1 + N_2 + 1) \quad (b) \end{array} \right\} \quad (835)$$

$$\left. \begin{array}{l} \text{and the variance } \sigma_{T_1}^2 = N_1 T_1 / 6 \quad \text{or} \quad (a) \\ \sigma_{T_1}^2 = 6 N_2 T_1 \quad (b) \end{array} \right\} \quad (846)$$

For samples outside the scope of the tables the following test quotient can be used

$$(T_1 - T_1) / \sqrt{\sigma_{T_1}^2} \quad \text{or} \quad (6 T_1 - 6 T_1) / \sqrt{\sigma_{T_1}^2} \quad (a) \quad (b) \quad (841)$$

Significance limit ϵ_α , page 28.

24C. The Wilcoxon test for pair differences³⁷ (Cf. section 9C, page 158)

The sum T_- is calculated in accordance with (836). The number of ranked pair differences is denoted by n (all zero values are ignored).

Significance limits for the sum T , are given in the table on page 128. If the differences have been calculated as $d_i = x_{1i} - x_{2i}$, and the sum T attains the significance limits or exceeds them in the outward direction from the expected value of T , then it follows that

$$\left. \begin{array}{l} \text{one-tailed test: } \left\{ \begin{array}{l} \mu_1 > \mu_2, \text{ when } T \leq T_1 (\leq \alpha) \\ \mu_1 < \mu_2, \text{ when } T \geq T_2 (\leq \alpha) \end{array} \right. \\ \text{two-tailed test } \mu_1 \neq \mu_2, \text{ when } T \leq T_1 \text{ or } T \geq T_2, \\ \quad (\leq 2\alpha) \end{array} \right\} \quad (842)$$

Under the null hypothesis, the expectation T of the estimate T is

$$T = n(n+1)/4 \quad (843)$$

and the variance is

$$\sigma_T^2 = (2n+1)T/6 \quad (844)$$

For samples outside the scope of the tables the following test quotient can be used,

$$(T - T) / \sqrt{\sigma_T^2} \quad (845)$$

Significance limit α , page 28

24D. Haldane's test for chance order in series²⁴

question whether the mortality m , or success of, a particular operation in the same hospital is increasing or decreasing, and so on. The test was developed by HALDANE for such problems independently of WILCOXON.

(a) Investigation of a series T_E is calculated as in (837). N_i is the number of trials (births, operations, etc.) in which the event E has occurred. N_i is $N - N_i$, where N is the total number of trials in the series being investigated.

The significance limits for T_E are the same as those in section 24B, the interpretation, however, is completely different. One-tailed test. If T_E attains or exceeds the left limit, then the frequency decreases with increasing lateness in the series, if it attains or exceeds the right limit, the frequency increases. Two-tailed test. The order has an influence on the frequency.

If all the events in the series cannot be specified, the following sequence, for example, may arise

$$\left. \begin{array}{cccccccccccc} \text{Trial} & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 & 11 & 12 \\ & + & + & ? & - & + & ? & + & - & + & ? & + \\ O_E & & & & 3 & & & & 9 & & & \\ O_2 & & 4 & & & 7 & & & & 11 & & \end{array} \right\} \quad (847)$$

and the tables on pages 124-127 can no longer be used. In such cases the test criterion (841b) is used, with

$$\left. \begin{array}{l} 6 T_E = 6 \Sigma O_E \quad (a) \\ 6 T_E = 6 N_i A / N \quad (b) \\ \sigma_{T_E}^2 = 36 N_i N_j (N B - A^2) / N^3 (N-1) \quad (c) \\ A = N(N+1)/2 - \Sigma O_i \quad (d) \\ B = N[1 + N(2N+3)]/6 - \Sigma O_i^2 \quad (e) \end{array} \right\} \quad (848)$$

If all the events are specified but the sample exceeds the scope of the table, then equations (839b) and (840b) can be used in conjunction with (841b).

(b) Investigation of several series as samples from the same population. The successive offspring of 1, 2, 3, ..., m mothers, for example, are to be investigated in respect of a childhood disease that appears to be commoner among later births.

The test criterion (841b) is used, with

$$\left. \begin{array}{l} 6 T = \Sigma 6 T_i \\ 6 T = \Sigma 6 T_i \\ \sigma_{T_i}^2 = \Sigma \sigma_{T_i}^2 \end{array} \right\} \quad (849)$$

$6 T_i$ and $\sigma_{T_i}^2$ are calculated from (839b) and (840b) or from (848b) and (848c) respectively, according to whether all the events in the series i are specified or not.

24E. The maximum test for pair differences^{25,26}

(This name was proposed by E. WALTER. The test is described here since it is also useful for assessing series, though by a method different to that of the WILCOXON test.)

With paired observations from continuous populations of any form the pair differences d_i are calculated as in section 16D, page 173. All zero values of d_i are excluded and the remainder arranged in the order of their absolute magnitudes. If two differences of equal absolute magnitude but opposite sign appear, then in order to be on the safe side these are so arranged that any runs of the same sign are as small as possible. The k differences with the highest absolute magnitude and the same sign are then counted.

The significance probability for a difference between the two series of measurements (two-tailed test) is then $2\alpha \approx (3/5)^k - 1$, that is,

$$\left. \begin{array}{lll} k = & 2\alpha = & \alpha = \\ 5 & 0.0625 \sim 0.1 & 0.03125 \sim 0.05 \\ 6 & 0.03125 \sim 0.05 & 0.015625 \sim 0.02 \\ 8 & 0.0078125 \sim 0.01 & 0.00390625 \sim 0.005 \\ 11 & 0.0009725 \sim 0.001 & 0.00048625 \sim 0.0005 \end{array} \right\} \quad (850)$$

Example 73. The series +3, 2, +2, 0, +1, 0, +1, 0, +7, +0.5, -0.3, +0.3 (note the awkward position of -0.3) results in a significance probability of $2\alpha \approx 0.05$.

25. Testing for non-randomness

25A. The mean-square successive difference²⁷

The mean-square successive difference δ^2 is defined as

$$\delta^2 = \frac{1}{N-1} \sum_{i=1}^{N-1} (x_{i+1} - x_i)^2; N = \text{size of the sample} \quad (851)$$

If the sample originates from a normally distributed population, then

$$\text{Expectation of } \delta^2 = 2\sigma^2 \quad (852)$$

$\delta^2/2$ is thus an unbiased estimate of σ^2 with

$$\text{Efficiency} = 2/3 [1 + 1/(3N-4)] \quad (853)$$

For $N=2$, the efficiency is therefore unity; for $N \rightarrow \infty$ (asymptotically) it is $2/3$.

Since the mean-square successive difference is calculated on the basis of the series x_1, x_2, \dots, x_N ,

$$\left. \begin{array}{l} \text{The ratio } \eta = \frac{\delta^2}{s^2} = \frac{\sum_{i=1}^{N-1} (x_{i+1} - x_i)^2}{\sum_{i=1}^N (x_i - \bar{x})^2} \end{array} \right\} \quad (854)$$

is therefore an indication of a possible non-random influence on the mean of a normally distributed population.

Significance limits for η are given in table 25A.1. (855)

The approximate limits ($N > 60$) in the table on page 58 have been calculated from

$$\eta_{1-\alpha} \approx 2 \mp 2 \sqrt{\frac{N-2}{(N-1)(N+1)}} \quad (856)$$

with empirical correction at the transition from exact to approximate values.

25B Serial correlation²⁸

known as the lag. For $i+h > N$, $x_{i+h} = x_{i+h-N}$ in the cyclic definition. For further details the reader is referred to the literature^{41, 42}.

With the cyclic definition, serial correlation is a sensitive instrument for revealing periodic influences on a population (or sample when the population is stable).

A measure of the serial correlation with lag h is the serial correlation coefficient R_h . Its estimate is

$$R_h = \frac{\sum x_i x_{i+h} - N \bar{x}^2}{\sum (x_i - \bar{x})^2} \quad (857)$$

As with other correlation coefficients, its value lies between -1 and $+1$.

The right-hand table on page 58 gives the significance limits for $R_h = 0$ (when $h = 1$) on the assumption that the samples are random samples from a normally distributed population. The approximate limits ($N > 75$) have been calculated from

$$R_{1r}, R_{1r} = \frac{-1 \pm |t_{\alpha}| \sqrt{N-2}}{N-1} \quad (858)$$

(N = number of values x_i included in the calculation)

with empirical correction at the transition from exact to approximate values. With this approximation the user remains on the safe side.

For lags other than 1 the same levels can be used, provided that h and N do not possess a common factor. The latter is always the case when N is a prime number. In practice these conditions can be met by deleting one or more individual sample values.

25C. Runs up and down^{43, 44}

If $x_1, x_2, \dots, x_i, \dots, x_N$ are individual sample values from a continuous population of any form, then a run up of length 1 is defined as the sequence $x_i \rightarrow x_{i+1}$ when $x_{i+1} - x_i > 0$. For runs down, $x_{i+1} - x_i < 0$. A sequence of three runs up of length 1 is called a run up of length 3, and so on.

If the sample is a random one not subject to cyclic or constant non-random influences, then the runs up and down should present a random picture, that is to say, there should be no regular runs and not too many long ones or too few short ones.

Runs up and down can be tested by means of the table at the foot of page 130. Thus a run of length 5 in a sample of size $N = 9$, for example, is not likely to be random ($\alpha = 0.01$). In the same way, sample of size $N = 12$ is not likely to be a random sample when a run of length 2 is present (significance probability $1 - 0.99 = 0.01$).

The number $I(I/N)$ of runs up and down of length I and the number $I(I+1/N)$ of runs of length I and longer can be regarded as normally distributed from $N = 20$ onwards. This can be tested by means of the quotient

$$(I - \bar{I})/\sqrt{\sigma_I^2}; \text{ significance level } |t_{\alpha}|, \text{ page 28} \quad (859)$$

The expected value \bar{I} and the variance σ_I^2 are functions of N ; appropriate formulae are to be found in the literature⁴⁵. To some extent their calculation is a tedious operation. The two tables (860) and (861) above give values up to the length usually found in practice; they also show clearly how σ^2 for greater lengths converges rapidly toward the expected value \bar{I} . It follows from (789) that the distribution of runs up and down very closely approximates, for runs of greater length, to a Poisson distribution (or to approximations to a Poisson distribution) with $\lambda = \bar{I}$.

25D. Runs above and/or below the median⁴⁵

Runs above and/or below the median can be tested by means of the table on page 130, where a brief explanation of the method will be found.

25E. Runs in samples from binomially distributed populations in which the probabilities p and q are unknown

The definition is as follows:

(Time)	1	2	3	4	5	6	7	8	9	10
Series (I)	<u>A</u>	<u>B</u>	<u>A</u>	<u>A</u>	<u>A</u>	<u>B</u>	<u>B</u>	<u>A</u>	<u>B</u>	<u>A</u>
Series (II)	<u>A</u>	<u>B</u>	<u>A</u>	<u>B</u>	<u>A</u>	<u>A</u>	<u>B</u>	<u>A</u>	<u>B</u>	<u>A</u>
Series (III)	<u>A</u>	<u>A</u>	<u>A</u>	<u>A</u>	<u>A</u>	<u>A</u>	<u>B</u>	<u>B</u>	<u>B</u>	<u>B</u>

Each of the series (I), (II), (III) has a size $N = 10$ and contains $N_1 = 4$ B's and $N_2 = 6$ A's (provided that $N = N_1 + N_2 < 40$, the smaller number is denoted by N_1). In these series the underscored

Expected value $\bar{I}(I/N)$ and variance of runs up and down of length I

Length	Expected value $\bar{I}(I/N)$			Variance $\sigma_I^2 = d \times \bar{I}(I/N) + e$		Remarks
	Exact $\bar{I}(I/N) = aN - b$		Asymptotic $\bar{I}(I/N) \rightarrow \bar{I}(1+1/N) \times e$ ($N \rightarrow \infty$)	d	e	
I	a	b	e			Note
1	$4.1\bar{6} \times 10^{-1}$	-8.3×10^{-2}	6.25×10^{-1}	1.016	-0.3972	— for b and e
2	$1.8\bar{3} \times 10^{-1}$	2.3×10^{-2}	2.75×10^{-1}	0.614550	-0.01943342	— for e
3	$5.2\bar{7} \times 10^{-2}$	$1.30\bar{5} \times 10^{-2}$	$7.91\bar{6} \times 10^{-2}$	0.794215	0.00678218	
4	$1.1507936\bar{5} \times 10^{-2}$	$4.12698413 \times 10^{-3}$	$1.72619048 \times 10^{-2}$	0.935800	0.00083924	
5	$2.0337301\bar{6} \times 10^{-3}$	$9.47420634 \times 10^{-4}$	$3.05059524 \times 10^{-3}$	0.985361	0.00004629	
6	$3.03130511 \times 10^{-4}$	$1.73059965 \times 10^{-4}$	$4.54695767 \times 10^{-4}$	0.997338	0.00000156	
7	$3.91313933 \times 10^{-5}$	$2.63999118 \times 10^{-5}$	$5.86970899 \times 10^{-5}$	0.999595	0.00000004	
8	$4.45927529 \times 10^{-6}$	$3.46721180 \times 10^{-6}$	$6.68891294 \times 10^{-6}$	0.999947	0.00000000	
9	$4.55113302 \times 10^{-7}$	$4.00416199 \times 10^{-7}$	$6.82669553 \times 10^{-7}$	0.999994	0.00000000	
10	$4.20746948 \times 10^{-8}$	$4.13038607 \times 10^{-8}$	$6.31120422 \times 10^{-8}$	0.999999	0.00000000	

Expected value $\bar{I}(I+1/N)$ and variance of runs up and down of length I and longer

Length	Expected value $\bar{I}(I+1/N)$			Variance $\sigma_I^2 = d \times \bar{I}(I+1/N) + e$		Remarks
	Exact $\bar{I}(I+1/N) = aN - b$		Asymptotic $\bar{I}(I+1/N) \rightarrow \bar{I}(1+1/N) \times e$ ($N \rightarrow \infty$)	d	e	
$I+$	a	b	e			Note
1	6.6×10^{-1}	3.3×10^{-1}	1	0.26	-0.23	— for e
2	2.5×10^{-1}	$4.1\bar{6} \times 10^{-1}$	3.75×10^{-1}	0.316	0.072	
3	6.6×10^{-2}	$1.8\bar{3} \times 10^{-1}$	1	0.710847	0.01729497	
4	1.38×10^{-2}	$5.2\bar{7} \times 10^{-2}$	$2.08\bar{3} \times 10^{-1}$	0.917857	0.00147817	
5	$2.3809\bar{5} \times 10^{-3}$	$1.1507936\bar{5} \times 10^{-2}$	$3.5714285\bar{7} \times 10^{-2}$	0.982145	0.00007053	
6	$3.47\bar{2} \times 10^{-4}$	$2.0337301\bar{6} \times 10^{-3}$	$5.208\bar{3} \times 10^{-3}$	0.996871	0.00000220	
7	$4.40917108 \times 10^{-5}$	$3.03130511 \times 10^{-4}$	$6.61375661 \times 10^{-4}$	0.999535	0.00000005	
8	$4.96031746 \times 10^{-6}$	$3.91313933 \times 10^{-5}$	$7.44047619 \times 10^{-5}$	0.999940	0.00000000	
9	$5.01042167 \times 10^{-7}$	$4.45927529 \times 10^{-6}$	$7.51563251 \times 10^{-6}$	0.999993	0.00000000	
10	$4.59288653 \times 10^{-8}$	$4.55113302 \times 10^{-7}$	$6.88932980 \times 10^{-7}$	0.999999	0.00000000	
11	$3.85417052 \times 10^{-9}$	$4.20746948 \times 10^{-8}$	$5.78125578 \times 10^{-8}$	0.999999	0.00000000	

is in each case form a run. The total number of runs I is 7 in

-) If the left limit is *attained* or *exceeded*, then I is significantly less than I (significance probability α) or differs significantly from I (significance probability 2α)
 c) If the right limit is *attained* or *exceeded*, then I is significantly greater than I (significance probability α) or differs significantly from I (significance probability 2α)
 c) If I lies between the limits and *attains neither*, then the null hypothesis cannot be rejected
 for N_1 and N_2 values outside the scope of the table, the test (859) can be used in conjunction with (848a) and (848b).

Expected values and variances

for the number of runs of length l of the event 1 that has occurred total of N_1 times (N_2 = number of events 2, $N = N_1 + N_2$)

$$I_1(l | N_1, N_2) = N_1(N_1 + 1) \frac{N_2!(N-l-1)!}{N!(N_1-l)!} \quad (a) \quad (862)^{**}$$

$$\sigma^2 = I \left[1 - I + N_2(N_2 - 1) \frac{(N-2l-2)!(N_1-l)!}{(N-l-1)!(N_1-2l)!} \right] \quad (b)$$

and asymptotically for higher values of N

$$I_1(l | N_1, N_2) = N p^l q^1 \quad (a) \quad (863)^{**}$$

$$\sigma^2 = I \left[1 - \frac{I}{N} \left[\frac{l^2}{p} + \frac{2}{q} - (l+1)^2 \right] \right] \quad (b)$$

for the number of runs of length l and longer of the event 1

$$I_1(l+1 | N_1, N_2) = (N_1 + 1) \frac{N_2!(N-l)!}{N!(N_1-l)!} \quad (a) \quad (864)^{**}$$

$$\sigma^2 = I \left[1 - I + N_2 \frac{(N-2l)!(N_1-l)!}{(N-l)!(N_1-2l)!} \right] \quad (b)$$

and asymptotically

$$I_1(l+1 | N_1, N_2) = N p^l q \quad (a) \quad (865)^{**}$$

$$\sigma^2 = I \left[1 - \frac{I}{N} \left[\frac{l^2}{p} + \frac{1}{q} \right] \right] \quad (b)$$

for the total number of all runs of the event 1

$$I_1(\text{total} | N_1, N_2) = I_1(1 + | N_1, N_2) = \frac{N_1(N_1 + 1)}{N} \quad (a) \quad (866)^{**}$$

$$\sigma^2 = \frac{I(I-1)}{N-1} \quad (b)$$

and asymptotically

$$I_1(\text{total} | N_1, N_2) = I(1 + | N_1, N_2) = N p q \quad (a) \quad (867)^{**}$$

$$\sigma^2 = I^2 / N \quad (b)$$

for the total number of all runs of events 1 and 2

$$I_{1+2}(\text{total} | N_1, N_2) = \frac{2 N_1 N_2}{N} + 1 \quad (a) \quad (868)^{**}$$

$$\sigma^2 = \frac{(I-1)(I-2)}{N-1} \quad (b)$$

and asymptotically

$$I_{1+2}(\text{total} | N_1, N_2) = 2 N p q \quad (a) \quad (869)^{**}$$

$$\sigma^2 = I^2 / N \quad (b)$$

The total number of all runs of the event 1 can be tested exactly (within the scope of the tables on pages 109-123) by means of the fourfold table test:

$$\left. \begin{array}{cc|c} I_1 & N_1 - I_1 & N_1 \\ N_1 + 1 - I_1 & I_1 - 1 & N_2 \\ \hline N_1 + 1 & N_1 - 1 & N \end{array} \right\} \quad (870)$$

25F The Wald-Wolfowitz test

Given are two samples from *continuous* populations of any form. These are ranked as in (833) and the total number of all runs (a run being defined as the occurrence of *successive* rank numbers in a sample) counted. Testing is carried out by means of the table on

page 129 (cf. section 25E) or, for samples outside the scope of the table, by means of the test quotient (859) in conjunction with (848a and b) or (849a and b).

Example 74. Ranking and determination of runs (1, 2, ... is the rank order):

Sample 1	1.55	1.58	1.70			1.92			2.20	2.21	
Sample 2				1.91		1.93	2.00				2.30
Order	1	2	3	4	5	6	7	8	9	10	11
Run 1 and 2	1		1	1	1		1		1		1
Total runs	6										

If the total number of runs *attains* or *passes* the left limit (on this limit can be used in this test), then the samples do not originate from the same population (significance probability 2α).

25G. Runs in samples from binomially distributed population in which the probabilities p and q are known

Expected values and variances

for the number of runs of length l of the event 1 the probability of whose occurrence is p ($q = 1 - p$)

$$I_1(l | N, p) = p^l q \quad (a) \quad (871)^{**}$$

$$\sigma^2 = I(1 - I) \quad (b) \quad (872)^{**}$$

$$I_1(l \leq N-1 | N, p) = p^l q [(N-l)q + 2] \quad (c) \quad (873)^{**}$$

$$\sigma^2 = I(1 - I) + \varphi(N, l) \quad (d) \quad (874)^{**}$$

where

$$\varphi(N, l) = 0; 2l \geq N \quad (e) \quad (875)^{**}$$

$$\varphi(N, l) = p^l q^2 [6 + 6(N-2l-2)q + (N-2l-2) \times (N-2l-3)q^2], 2 \leq 2l \leq N-2 \quad (f) \quad (876)^{**}$$

$$\varphi\left(N, \frac{N-1}{2}\right) = 2p^{N-1}q, N \text{ odd} \quad (g) \quad (877)^{**}$$

and asymptotically when $N \rightarrow \infty$

$$I_1(l | N, p) = N p^l q^2 \quad (a) \quad (878)^{**}$$

$$\sigma^2 = I \left[1 - p^l q^2 \left[2 \left(l - \frac{2l}{q} \right) + 1 \right] \right] \quad (b) \quad (879)^{**}$$

for the number of runs of length l and longer

$$I_1(l+1 | N, p) = p^l [(N-l)q + 1] \quad (a) \quad (880)^{**}$$

$$\sigma^2 = I(1 - I) + \psi(N, l) \quad (b) \quad (881)^{**}$$

where

$$\psi(N, l) = 0, 2l \geq N \quad (c) \quad (882)^{**}$$

$$\psi(N, l) = p^l q [(N-2l) \{ 2 + (N-2l-1)q \}], 2 \leq 2l \leq N \quad (d) \quad (883)^{**}$$

and asymptotically when $N \rightarrow \infty$

$$I_1(l+1 | N, p) = N p^l q \quad (a) \quad (884)^{**}$$

$$\sigma^2 = I[1 - p^l q(2l+1)] \quad (b) \quad (885)^{**}$$

for the total number of runs of the event 1

$$I_1(\text{total} | N, p) = p [(N-1)q + 1] \quad (a) \quad (886)^{**}$$

$$\sigma^2 = I(1 - I) + (N-2)p^l q [(N-3)q + 2] \quad (b) \quad (887)^{**}$$

and asymptotically

$$I_1(\text{total} | N, p) = N p q \quad (a) \quad (888)^{**}$$

$$\sigma^2 = I(1 - 3 p q) \quad (b) \quad (889)^{**}$$

for the total number of runs of events 1 and 2

$$I_{1+2}(\text{total} | N, p) = 2(N-1)pq + 1 \quad (a) \quad (890)^{**}$$

$$\sigma^2 = 2pq[2\{N - (3N-5)pq\} - 3] \quad (b) \quad (891)^{**}$$

and asymptotically

$$I_{1+2}(\text{total} | N, p) = 2 N p q \quad (a) \quad (892)^{**}$$

$$\sigma^2 = I(2 - 3 p q) \quad (b) \quad (893)^{**}$$

25H. Runs in samples from multinomially distributed populations

(a) The probabilities $p_1, p_2, \dots, p_k, \dots, p_s$ are unknown

Expected values and variances

for the total number of runs of the event i that has occurred total of N_i times

$$I_i(\text{total} | N_i, N) = \frac{N_i(N - N_i + 1)}{N} \quad (a) \left. \vphantom{\frac{N_i(N - N_i + 1)}{N}} \right\} (879)^{46}$$

$$\sigma^2 = \frac{I(I-1)}{N-1} \quad (b)$$

and asymptotically

$$I_i(\text{total} | N_i, N) = Np_i(1 - p_i) \quad (a) \left. \vphantom{Np_i(1 - p_i)} \right\} (880)^{46}$$

$$\sigma^2 = \frac{I^2}{N} \quad (b) \quad p_i = \frac{N_i}{N}$$

– for the total number of runs of all events

asymptotically

$$I(\text{total}, N) = N(1 - \sum_{i=1}^k p_i^2) \quad (a) \left. \vphantom{N(1 - \sum_{i=1}^k p_i^2)} \right\} (881)^{46}$$

$$\sigma^2 = N[\sum p_i^4 - 2\sum p_i^2 + (\sum p_i^2)^2] \quad (b)$$

When $N_1 = N_2 = \dots = N_k = N_0$, (881) becomes

$$I(\text{total}) = N(1 - p) \quad (a) \left. \vphantom{N(1 - p)} \right\} (882)$$

$$\sigma^2 = pI \quad (b) \quad p = 1/k; N = kN_0$$

(b) The probabilities p_i are known

p_i is the probability that the event i will occur.

Expected values and variances

– for the total number of runs of the event i

$$I_i(\text{total} | N, p_i) = p_i[(N-1)(1-p_i) + 1] \quad (a) \left. \vphantom{p_i[(N-1)(1-p_i) + 1]} \right\} (883)^{46}$$

$$\sigma^2 = Np_i(1-4p_i+6p_i^2-3p_i^3) + p_i^2(3-8p_i+5p_i^2) \quad (b)$$

[Formula (883) is identical with (875) when, in the latter, p is replaced by p_i]

and asymptotically

$$I_i(\text{total} | N, p_i) = Np_i(1 - p_i) \quad (a) \left. \vphantom{Np_i(1 - p_i)} \right\} (884)^{46}$$

$$\sigma^2 = I[1 - 3p_i(1 - p_i)] \quad (b)$$

– for the total number of runs of all events

asymptotically

$$I(\text{total}) = N(1 - \sum p_i^2) \quad (a) \left. \vphantom{N(1 - \sum p_i^2)} \right\} (885)^{46}$$

$$\sigma^2 = N[\sum p_i^4 + 2\sum p_i^2 - 3(\sum p_i^2)^2] \quad (b)$$

When $p_1 = p_2 = \dots = p_k = p = 1/k$, (885) becomes

$$I(\text{total}) = N(1 - p) \quad (a) \left. \vphantom{N(1 - p)} \right\} (886)^{46}$$

$$\sigma^2 = pI \quad (b)$$

26. Sequential analysis

Sequential analysis is one of the more recently developed statistical methods, and its use in medical trials is increasing⁵¹. It is illustrated here by two charts⁵² that enable a comparison to be made, for example between two drugs, without calculation.

Example 75. The effect on patients of drug A is to be compared with that of drug B. Two patients are selected, the toss of a coin deciding which one is to receive drug A and which drug B. They should receive the drugs *simultaneously or in quick succession*. The result is given one of the three ratings

Drug A better Drug B better No difference

If drug A is better, a cross is made in the square immediately above the black square in the charts (Figs. 49 and 50). If drug B is better, a

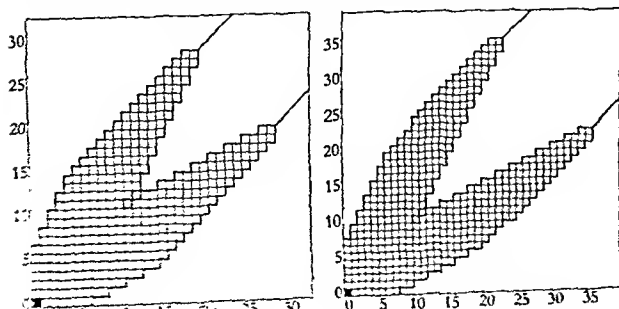


Fig. 49. Sequential analysis chart

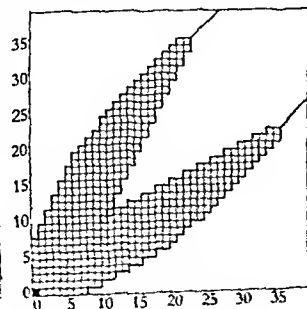


Fig. 50. Sequential analysis chart

cross is made in the square immediately to the right of the square. If there is no difference, no entry is made in the chart. The second test is then made in exactly the same way with two different patients and the result entered in the square above or to the right of that marked in the first test, and so on for successive tests. Associated with a barrier is overstepped one of the following decisions can be made:

- (a) upper barrier overstepped: drug A is better
- (b) lower barrier overstepped: drug B is better
- (c) middle barrier overstepped: no difference demonstrated

The significance probability for (a) and (b) combined is 2α .

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- Normal quantiles, standard deviation 165
- regressions, first kind 174 sq.
 - second kind 179 sq.
 - samples, and hypothetical population 171, 172
 - comparison of two 172, 173
 - distn., samples, testing of several 173, 174
 - quantiles, standard deviations 165
 - bivariate 179 sq.
 - logarithmic 165
 - standardized 162, 163
 - tables 29-31, 43-55, 58-65, 162
- Normal range 454, 455
- Null hypothesis 157
- Orthogonal regression coefficient 738
- Pair differences, tests of 158, 161, 173, 192, 196
- Parameters 159 sq.
- See also Mean, Mode, Quantiles, Variance
- Percentiles 499
- Poisson distribution 187 sq.
- addition theorem 786
 - arc-sine transformation 789
 - and binomial distribution 186
 - and χ^2 distribution 561-563
 - confidence limits, tables 107, 108
 - confidence limits and significance limits 189
 - parameters 188
 - and hypergeometric distribution 814
 - samples, frequency testing 192
 - significance limits, table 128
 - transformations 188, 189
- Populations, definition 318
- infinite 327, 328
 - normally distributed. See Normal distribution
 - unknown and hypothetical 464-466
 - See also Distributions
- Power of significance tests 157
- Probability, definitions 324, 350-423
- symbols 349
 - continuous distribution 151 sq.
 - cumulative, of binomial distribution 184, 185
 - Poisson distribution 148 sq.
 - 744
 - 805
 - of Poisson distribution 784
- Probability density function, definition 400
- of χ^2 distribution 554
 - 571
 - 532
 - of normal distribution 506
 - of standardized normal distribution 510
 - of Student distribution 549
 - of t -distribution 549
 - probit, empirical, calculation 164
 - probit line, fitted, calculation 164
 - regression 179
 - transformation 163, 164
 - tables 54, 55
- Quantiles of continuous distributions 160, 161
- distribution-free confidence limits 104, 161, 187
 - of samples, standard deviations 165
- Quartiles 489
- Random events 321
- numbers, table 131
 - variables. See under Variables
- Ranks, definition 342
- Rank correlation coefficient 181
- Tests 192, 193
- Ranking of samples 192, 342, 501
- Recursion formulae, for binomial distribution 745
- for hypergeometric distribution 807, 808
 - for Poisson distribution 785
- Regressions of 1st kind 174 sq.
- of 2nd kind 179 sq.
 - logit and probit 179
- Regression coefficient, testing against zero 177
- orthogonal 738
- Regression functions 174
- testing for linearity 176, 177
- Regression lines, 1st kind, comparison 178, 179
- estimates of parameters 174 sq.
 - estimates of x , given y 177, 178
 - parallel 689-692, 698-701
- Root-mean-square deviation. See Variance
- Runs, above and/or below the median 194
- up and down 194
 - in samples from binomial distributions 194, 195
 - in samples from multinomial distributions 195
 - fourfold table test for 195
 - length of 131
 - significance limits for total 130
- Samples, definition 322
- distributions, populations and 329
 - fitting normal curves to 163 sq.
 - ranking of 192, 342, 501
 - from binomial distributions, frequency test 191
 - size for given probability 187
 - grouped, estimates of mean and variance 160
 - fitting normal curves to 164
 - and lognormal distribution 544
 - from normal distributions, standard deviations of quantiles 165
 - from normal distributions, and hypothetical population 171, 172
 - tests for several 173, 174
 - tests for two, using extreme range 173
 - from multinomial and Poisson distributions, frequency tests 192
 - ungrouped, mean and variance estimates 159, 160
 - fitting normal curves to 164
 - and lognormal distribution 543
- Sampling, from finite and infinite populations 357
- random 320
 - with replacement 328
- Sequences, random 323
- testing of 193 sq.
 - ranked 342, 192
 - testing of 192, 193
- Sequential analysis 196
- Serial correlation 58, 193, 194
- SHEPPARD'S correction 498
- Sign test 158, 159, 161
- tables 104-106
- Significance limits 152, 156, 157
- convergence 462
 - of binomial distributions 186, 187
 - of continuous distributions, one-sided 409, 410
 - two-sided 417
 - of discrete distributions, one-sided 376, 377
 - two-sided 390
 - of hypergeometric distributions 109-123, 191
 - of normal distribution 58, 61
 - of Poisson distributions 189
 - in WILCOXON test 124-128, 193
 - for runs, table 129
- Significance probability (α , 2α) 376-379, 384, 390, 391, 409-412, 417-420
- See also under Tests
- SPEARMAN correlation coefficient 181
- Standard deviation. See under Variance
- Standardized extreme deviation 594
- extreme range 586, 588
 - normal distribution 162, 163
 - variables 489
- Statistically significant differences, meaning 159
- Stochastic convergence of estimates 153
- dependence of events 358, 361
 - independence of events 359, 361
- Student distribution 166
- tables 32-35, 42, 165
 - test (t -test) 158, 159, 599
- 'Studentized' extreme deviation 170
- extreme range 170
- Sums of squares 493, 634, 636, 643-654
- Symmetry of normal distribution 161
- of samples 162
- t -distribution (Student) 166
- t -test (Student) 158, 159, 599
- Test, BARTLETT'S 621, 622
- F 598
 - chi-squared (χ^2) 558, 565-569, 584, 721, 781, 825-828
 - for normal distribution 163-165
 - for Poisson distribution 188
 - for chronological order effect 193
 - of correlation coefficient r 179, 180
 - of serial correlation coefficient 857, 858
 - of SPEARMAN correlation coefficient 181
 - DUNCAN'S 627-630
 - of extreme values 170, 171
 - F 605
 - fourfold table 191, 870
 - of frequencies 191, 192
 - for goodness of fit 566, 567
 - HALDANE'S 193
 - LORD 158, 159, 600
 - maximum 158, 159, 193
 - midrange 158, 159, 601
 - for non-randomness 193 sq.
 - one-tailed and two-tailed 157, 158
 - of paired differences 158, 161, 173, 192, 196
 - of ranks 192, 193
 - rapid (normal distribution) 172
 - Test, of regressions of first kind 177
 - of regressions of second kind 181
 - for linearity of regression functions 176, 177
 - of runs 194
 - of chance order in series 193
 - of samples, from binomial populations 191
 - from multinomial populations 192
 - from normal populations 173
 - from Poisson populations 192
 - sign 158, 159, 161
 - significance 156 sq.
 - for correlation coefficients 180
 - for regressions of second kind 181, 182
 - for symmetry 162
 - t (Student) 158, 159, 599
 - for two samples using the extreme range 173
 - two-by-two (fourfold) table 191, 870
 - of variances 173
 - WALD-WOLFOWITZ 195
 - WALSH 158, 159, 602
 - WILCOXON, for pair differences 158, 192
 - for two samples 192
- Ties 346
- ranking of 834
- Tolerance ellipse of regressions of 2nd kind 737
- limits (factors, intervals) 154, 155
 - convergence of 449
 - distribution-free 128, 155, 156, 187
 - of continuous distributions 152
 - of discrete distributions 150
 - of normal distributions 44-46, 169
 - of regressions of first kind 669, 670, 674
 - of regressions of second kind 737
- Transformations 159
- arc-sine. See Arc-sine transformation
 - z , of correlation coefficient 180
 - See also under Approximations
- Tries 319
- Two-by-two (fourfold) table test 191
- Unbiased estimates of standard deviation 170
- Variables, definition 317
- and events 147
 - 'atomic' or 'granulated' 344-346
 - continuous 343
 - dependent and independent 179
 - discrete 341
 - random 339-346
 - standardized 489
- Variance (and standard deviation) 153 sq., 161, 162
- analysis of (normal distribution) 173, 174
 - BARTLETT'S test for 621, 622
 - and χ^2 distribution 565
 - confidence limits for 565, 584
 - convergence of 432
 - coefficient of 485
 - estimates of, based on grouped samples 160
 - based on ungrouped samples 159
 - unbiased 494, 170
 - and extreme range 170
 - F -test for 605
 - and mean-square successive difference 852, 853
 - and probit line 164
 - and CHERNSHEF inequality 486
 - of binomial distribution 184
 - of χ^2 distribution 555
 - of F -distribution 572
 - of hypergeometric distribution 812
 - of the mean 484, 495
 - of normal distribution 161, 171, 172, 173
 - confidence intervals for 169
 - of Poisson distribution 787-789
 - of the population 159
 - of rank sums (WILCOXON) 192, 193
 - in regressions 174, 175
 - of runs 194
 - of samples 159
 - and χ^2 distribution 565
- Variation, coefficient of 485
- WALD-WOLFOWITZ test 195
- WALSH test 158, 159, 602
- WILCOXON tests 158, 192, 193
- tables 124-128
- z -distribution 168
- z -transformation (of correlation coefficient) 180

- Normal quantiles, standard deviation..... 165
 - regressions, first kind 174 sq.
 - - second kind 179 sq.
 - samples, and hypothetical population. 171, 172
 - - comparison of two 172, 173
 - distn., samples, testing of several..... 173, 174
 - - quantiles, standard deviations 165
 - bivariate 179 sq.
 - logarithmic 165
 - standardized 162, 163
 - - tables 29-31, 43-55, 58-65, 162
- Normal range 454, 455
- Null hypothesis 157
- Orthogonal regression coefficient 738
- Pair differences, tests of .. 158, 161, 173, 192, 196
- Parameters 159 sq.
 - See also Mean, Mode, Quantiles, Variance
- Percentiles 499
- Poisson distribution 187 sq.
 - addition theorem..... 786
 - arc-sine transformation 799
 - and binomial distribution 186
 - and χ^2 distribution 561-563
 - confidence limits, tables..... 107, 108
 - confidence limits and significance limits... 189
 - parameters 188
 - and hypergeometric distribution..... 814
 - samples, frequency testing 192
 - significance limits, table..... 128
 - transformations..... 188, 189
- Populations, definition 318
 - infinite 327, 328
 - normally distributed. See Normal distribution
 - unknown and hypothetical 464-466
 - See also Distributions
- Power of significance tests 157
- Probability, definitions..... 324, 350-423
 - symbols 349
 - continuous distribution 151 sq.
 - cumulative, of binomial distribution . 184, 185
 - discrete distribution 148 sq.
 - individual, of binomial distribution 744
 - - of hypergeometric distribution 805
 - - of Poisson distribution..... 784
- Probability density function, definition 400
 - of χ^2 distribution..... 554
 - of F -distribution 571
 - of lognormal distribution..... 532
 - of normal distribution 506
 - of standardized normal distribution 510
 - of Student distribution 549
 - of t -distribution..... 549
- Probits, empirical, calculation 164
- Probit line, fitted, calculation..... 164
 - regression 179
 - transformation 163, 164
 - tables 54, 55
- Quantiles of continuous distributions .. 160, 161
 - distribution-free confidence limits 104, 161, 187
 - of samples, standard deviations..... 165
- Quartiles 499
- Random events 321
 - numbers, table..... 131
 - variables. See under Variables
- Ranks, definition..... 342
- Rank correlation coefficient..... 181
 - tests 192, 193
- Ranking of samples..... 192, 342, 501
- Recursion formulae, for binomial distribution 745
 - for hypergeometric distribution 807, 808
 - for Poisson distribution 785
- Regressions of 1st kind..... 174 sq.
 - of 2nd kind 179 sq.
 - logit and probit 179
- Regression coefficient, testing against zero .. 177
 - orthogonal..... 738
- Regression functions 174
 - testing for linearity 176, 177
- Regression lines, 1st kind, comparison . 178, 179
 - - estimates of parameters 174 sq.
 - - estimates of x , given y 177, 178
 - - parallel 689-692, 698-701
- Root-mean-square deviation. See Variance
- Runs, above and/or below the median 194
 - up and down 194

(Combinations and multiples of symbols like cm, m³, km h⁻¹, etc are not included)

	Page		Page		Page
(sexagesimal) minute	207	F	farad	216	O
(sexagesimal) second	207	*F	degree Fahrenheit	209	osm
degree	207				ounce
square degree	207	G	grade	207	Oe
right angle	207	g	gramme	204, 213	Ω
		gal	gallon	203	Ω ⁻¹
		gf	gramme-force	211	
are	203	gi	gill	204	P
atto- (10 ⁻¹⁸)	9	gr	gram	204	p
year (astronomy)	206	grf	gram-force	211	pc
atomic mass unit (old)	227	G	giga- (10 ⁹)	9	pdl
apothecaries' (measures)	205	Gal	galileo	210	phon
apothib	223	Gb	gilbert	216	phot
technical atmosphere	212	Gs	gauss	216	pk
physical atmosphere	212	γ (μg)	gamma* (microgramme)	204	pt
avoirdupois (measures)	205	H	hecto- (10 ²)	9	P
ampere	215, 216	h	hour	205	PS
astronomical unit	200	h	horsepower	214	
angstrom	200, 202	hp	horsepower	214	Q
		Hz	henry	216	qr
barn	202, 203	Hz	hertz (cycle per second)	208	qt
bar	211				
barrel	204	I	inch	200	R
bushel	203, 204	in	inch	200	r
British thermal unit	213	inHg	inch of mercury	212	r
		inH ₂ O	inch of water	212	rad
centesimal minute	207	J	joule	212, 213, 216	rd
centi- (10 ⁻²)	9	K	kilo- (10 ³)	9	sd
cycle per second	208	k	kilogramme-force	211	rem
15° calorie	213	kgf	knot	200	R
Int Steam Table calorie	213	kn	knot	200	*R
thermochemical calorie	213	K	kelvin	208, 213	Ry
centesimal second	207	L	litre	203	S
candela	223	l	litre	203	s
chain	200	lb	pound	204	s ⁻¹
metric horsepower	213	lbf	pound-force	211	sb
reciprocal centimetre	213	li	link	200	sh cwt
hundredweight	205	liq pt	liquid pint	204	sh tn
coulomb	216	liq qt	liquid quart	204	sonc
degree Celsius (Centigrade)	208	lm	lumen	222	sr
cune	217	lx	lux	223	st
		ly	light year	201	St
deci- (10 ⁻¹)	9	L	lambert	223	
day	205	M	mega- (10 ⁶)	9	T
deca- (10 ¹)	9	m	metre	200	e
decibel	225	m	metre	200	t, tr
dram, drachm	205	mi	mile	200	ton
dry pint	204	min	minute	205	tonf
dry quart	204	min	minim	204	T
pennyweight	205	mmHg	millimetre of mercury	212	T
dyne	211	mmH ₂ O	millimetre of water	212	T
		mol	mole	226	torr
electromagnetic unit	215	M	mega- (10 ⁶)	9	U
erg	212, 213	Mx	maxwell	216	u
electrostatic unit	215	μ	micro- (10 ⁻⁶)	9	V
electron volt	213	μ (μm)	micron* (micrometre)	200	v
gramme-equivalent	226	N	nano- (10 ⁻⁹)	9	V
		n	nautical mile	200	v
femto- (10 ⁻¹⁵)	9	N	newton	211, 216	W
fathom	200				W
fluid dram (fluid drachm)	204				Wb
fluid ounce	204				
foot	200				X
foot of water	212				XU
furlong	200				Y
					yd

* This name and symbol should no longer be used

centimetre gramme second (system of units)
Comité International des Poids et Mesures
International Astronomical Union
International Commission on Radiological Units
and Measurements

IUPAC International Union of Pure and Applied Chemistry
IUPAP International Union of Pure and Applied Physics
MKS
MKSA
RBE

Length (l)

Dimension = L

Coherent units

International System of Units: metre (m)

CGS system: centimetre (cm)

ft-lb-s system: foot (ft)

International System of Units (SI units)[†]

The base (or 'basic') unit of length is the metre** (m). This was re-defined^{††} in 1960 as a multiple of the vacuum wavelength $\lambda(^{86}\text{Kr})$ of the orange-red spectral line of the atom of krypton-86, as follows: The metre is the length equal to 1 650 763.73 wave lengths in vacuum of the radiation corresponding to the transition between the levels $2p_{10}$ and $5d_5$ of the krypton-86 atom. The re-defined metre is therefore based on a natural quantity, namely the energy difference between two electron terms of an unperturbed atom. It follows that

$$\lambda(^{86}\text{Kr}) = 6.057\,802\,21 \times 10^{-7} \text{ metre}$$

For the history of the metre as a unit see the literature².

Secondary standards³(a) Vacuum wave lengths of the krypton nuclide ^{86}Kr

$$2p_9 - 5d_4': 6.458\,072\,0 \times 10^{-7} \text{ m}$$

$$2p_8 - 5d_4: 6.422\,800\,6 \times 10^{-7} \text{ m}$$

$$1s_3 - 3p_{10}: 5.651\,128\,6 \times 10^{-7} \text{ m}$$

$$1s_4 - 3p_8: 4.503\,616\,2 \times 10^{-7} \text{ m}$$

(b) Vacuum wave lengths of the mercury nuclide ^{198}Hg

$$6^1P_1 - 6^1D_2: 5.792\,268\,3 \times 10^{-7} \text{ m}$$

$$6^1P_1 - 6^3D_2: 5.771\,198\,3 \times 10^{-7} \text{ m}$$

$$6^3P_2 - 7^3S_1: 5.462\,270\,5 \times 10^{-7} \text{ m}$$

$$6^3P_1 - 7^3S_1: 4.359\,562\,4 \times 10^{-7} \text{ m}$$

(c) Vacuum wave lengths of the cadmium nuclide ^{114}Cd

$$5^1P_1 - 5^1D_2: 6.440\,248\,0 \times 10^{-7} \text{ m}$$

$$5^3P_2 - 6^3S_1: 5.087\,237\,9 \times 10^{-7} \text{ m}$$

$$5^3P_1 - 6^3S_1: 4.801\,252\,1 \times 10^{-7} \text{ m}$$

$$5^3P_0 - 6^3S_1: 4.679\,458\,1 \times 10^{-7} \text{ m}$$

Conversion of metric units of length

		1 A unit = b B units (b in the table)						
A		B						
Name	Symbol	nm	μm	mm	cm	dm	m	km
ångström	Å	10^{-1}	10^{-4}	10^{-7}	10^{-8}	10^{-9}	10^{-10}	10^{-13}
nanometre	nm	1	10^{-3}	10^{-6}	10^{-7}	10^{-8}	10^{-9}	10^{-12}
(millimicron) [†]	(m μ t)							
micrometre	μm	10^3	1	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-9}
(micron) [†]	(μ t)							
millimetre	mm	10^6	10^3	1	10^{-1}	10^{-2}	10^{-3}	10^{-6}
centimetre	cm	10^7	10^4	10	1	10^{-1}	10^{-2}	10^{-5}
decimetre	dm	10^8	10^5	10^2	10	1	10^{-1}	10^{-4}
metre	m	10^9	10^6	10^3	10^2	10	1	10^{-3}
decametre	dam	10^{10}	10^7	10^4	10^3	10^2	10	10^{-2}
hectometre	hm	10^{11}	10^8	10^5	10^4	10^3	10^2	10^{-1}
kilometre	km	10^{12}	10^9	10^6	10^5	10^4	10^3	1

[†] In accordance with a resolution of the 13th General Conference of Weights and Measures (1967), these names and symbols, formerly in common use, should no longer be used.

Anglo-Saxon systems of measurement

The primary standard of length in the Anglo-Saxon systems of measurement is the *yard* (yd), though the coherent length unit in the ft-lb-s system is the foot (ft) = $\frac{1}{3}$ yard. Recently the yard has been defined in terms of the metre as follows⁴:

$$1 \text{ yard} = 0.9144 \text{ m} = 1.509\,458\,3_s \times 10^6 \lambda(^{86}\text{Kr})$$

* This chapter (pages 200-227) has been compiled in collaboration with G. BECKER, W. FRITZ, J. HUNTER-BLANCK, W. KUNER, H. STILLE, H.-M. WELZ, Braunschweig, and S. BÖHME, Heidelberg.

** In the USA, 'meter'.

This newly defined 'unified' yard[†] lies between the former imperial yard of the United Kingdom⁵ and the former US yard⁶:

$$1 \text{ imperial yard} = 0.914\,398\,41 \text{ m} < 1 \text{ unified yard} < 1 \text{ US yard} = (36/39.37) \text{ m} = 0.914\,401\,83 \text{ m}^{††}$$

Conversion of Anglo-Saxon units of length

		1 A unit = b B units (b in the table)		
A		B		
Name	Symbol	yd	ft	m
mil	—	1/36 000	1/12 000	2.54×10^{-5}
point (printers') (US) [†]	—	—	—	3.515×10^{-4}
line (button) (US) ...	—	1/1440	1/480	6.35×10^{-4}
inch	in	1/36	1/12	2.54×10^{-2}
hand (US)	—	1/9	1/3	1.016×10^{-1}
link	li ^{††}	22/100	66/100	$2.011\,68 \times 10^{-1}$
span (US)	—	1/4	3/4	2.286×10^{-1}
foot	ft	1/3	1	3.048×10^{-1}
yard	yd	1	3	9.144×10^{-1}
fathom	fath ^{††}	2	6	1.828 8
rod (pole, perch)	rd ^{††}	11/2	33/2	5.029 2
chain	ch ^{††}	22	66	$2.011\,68 \times 10$
furlong	fur. ^{††}	220	660	$2.011\,68 \times 10^2$
(statute) mile	mile ^{†††}	1760	5280	$1.609\,344 \times 10^3$

[†] Definition: 1 point (printers') (US) = 0.013 837 in.

^{††} Symbols in use only in USA.

^{†††} Symbol in USA: mi.

Nautical and geodetic units of length

The *nautical mile* is defined as the length of the mean minute of arc on the meridian of the earth (mean minute of latitude). When the values of the terrestrial polar and equatorial radii derived from the international terrestrial geoid⁷ are used

$$1 \text{ nautical mile} = \frac{\text{quadrant of meridian } Q_{\text{Me}}^{\text{Me}}}{90 \times 60} = 1852.276 \text{ m}$$

In 1928 the International Hydrographic Conference in Monaco proposed the following international unified definition⁸:

$$1 \text{ international nautical mile} = 1852 \text{ m}$$

This value was accepted by all maritime nations (by USA in 1954⁹) with the exception of the United Kingdom, where the nautical mile is based on the knot:

$$1 \text{ Admiralty knot} = \frac{1 \text{ nautical mile}}{\text{hour}} = 6080 \text{ imperial feet per hour}$$

whence

$$1 \text{ imperial nautical mile (n mile)} = 1853.181 \text{ m}$$

The *geographical mile* (not to be confused with the land, or statute, mile) is now based on the equatorial quadrant Q_{E}^{E} (Δ 4 minutes of arc) on the equator). When the value of the terrestrial equatorial radius derived from the international terrestrial geoid⁷ is used

$$1 \text{ geographical mile} = 4 \times \frac{\text{equatorial quadrant } Q_{\text{E}}^{\text{E}}}{90 \times 60} = 7421.591 \text{ metres}$$

Astronomical units of length

In astronomy the unit of length is the *astronomical unit* (AU). This is based on a definition requiring some preliminary explanation. With the ephemeris day (d) of 86 400 ephemeris seconds (s) as time unit and the mass of the sun (M_{s}) as mass unit the undisturbed elliptical ('KEPLER') path of a planet is characterized by

- n the sidereal mean daily motion (angular velocity) in rad/d
- \bar{m} the mass in M_{s}
- a the semi-major axis in AU
- k the GAUSS gravitational constant in $(\text{AU})^{3/2} \text{ rad d}^{-1} M_{\text{s}}^{-1/2}$

[†] Formerly also called 'international yard' in English-speaking countries.
^{††} In the US Coast and Geodetic Survey the foot legally defined in 1886 and 1893⁶ /US Survey Foot = $12/39.37 \text{ m} \approx 0.304\,800\,609 \text{ m}$ retains its validity, for instance for the basic geodetic survey networks of the United States (see National Bureau of Standards⁴).

The AU is then defined as that unit in which the quantity a is measured in KEPLER's Third Law $a^3/a^3 = k^3(1 + \bar{m})$ (an equation between numerical values) with the conventionally agreed numerical value $k = na^{3/2} = 0.01720209895$ for the GAUSS gravitational constant, measured in $(\text{AU})^{3/2} \text{ rad d}^{-1} M_\odot^{-1/2}$. The AU is thus a derived unit determined by the units chosen for time and mass and the fixed value of the GAUSS constant k . It can be described as the

was the reason for GAUSS'S measurement of k , which the disturbing effects of the other planets are taken into account the value is 1 000 000 2 AU.

It is still necessary to express the AU as a multiple A of the metre or some other reference length. The former is obtained directly from radar measurements (up to now mainly of the planet Venus, whose distance is known from the ephemerides), determination of the solar parallax π_\odot measures the relationship of the AU to the equatorial radius a_e of the earth. The 'IAU System of Astronomical Constants' was laid down by the 12th General Assembly of the International Astronomical Union in 1964¹⁰ by assigning conventionally agreed values to the 'defining' and 'primary' constants. In this system

$$1 \text{ AU} = A \text{ m} = 149\,600 \times 10^3 \text{ m}$$

$$\pi_\odot = \arcsin(a_e/A \text{ m}) = 8\,794\,05'', \text{ with } a_e = 6\,378\,160 \text{ m}$$

Since radar measurements are measurements of time differences the time τ_A taken by light to travel 1 AU is also given, in the same system it is

$$\tau_A = (A \text{ m})/c = 499\,012 \text{ s, with } c = 299\,792\,5 \times 10^3 \text{ m s}^{-1} \text{ to 1 s}$$

In stellar astronomy the distances involved are far greater than those of the solar system ($> 2 \times 10^4$ AU), and more appropriate length units have been introduced, namely the parsec, light year and

parallax and second). Since $p < 0.8''$ for all stellar parallaxes, parallax and distance are related as follows

$$n \text{ pc} / 648\,000'' = 1 \text{ AU}$$

whence $r = 648\,000'' / (\pi p) \text{ AU}$

and $r = 1/p \text{ pc}$ by definition

$$\text{It follows that } 1 \text{ pc} = 648\,000/\pi \text{ AU} = 206\,264.8 \text{ AU}$$

$$\text{and } 1 \text{ pc} = 648\,000/\pi A \text{ m} = 3\,085\,72 \times 10^{12} \text{ km}$$

The larger units usually employed are

$$1 \text{ kpc} = 10^3 \text{ pc}, 1 \text{ Mpc} = 10^6 \text{ pc}$$

The *light year* (ly) is the distance travelled by light in one tropical year. When the values of the IAU System of Astronomical Constants¹⁰ for the velocity of light and the number of ephemeris seconds in 1 tropical year are used

$$1 \text{ ly} = 299\,792\,500 \text{ m s}^{-1} \times 31\,556\,925\,974\,7 \text{ s}$$

$$= 9\,460\,529\,73 \times 10^{12} \text{ km}$$

For objects whose parallax cannot be (more or less) directly measured, the *distance modulus* is used as indirect measure of distance

propagation of light in an absorption-free space

$$m - M = 5 \log_{10} (r/\text{pc}) - 5 = -5 - 5 \log_{10} (p'')$$

For $m - M = -5^m, 0^m, +5^m, +10^m, \dots +25^m$ the corresponding distances are $r = 1, 10, 100, 1000, \dots 10^5 \text{ pc}$

If M can be determined from the physical structure of the object, r or p can be obtained from

$$\log_{10} (r/\text{pc}) = 0.2 (m - M + 5) = -\log_{10} (p'')$$

Conversion of astronomical units of length¹¹

		1 A unit = k B units (k in the table)		
A		B		
Name	Symbol	AU	pc	ly
astronomical unit	AU	1	$4\,848\,14 \times 10^{-6}$	$1\,581\,31 \times 10^{-8}$
parsec	pc	$2\,062\,648 \times 10^3$	1	$3\,261\,68$
light year	ly	$6\,323\,88 \times 10^4$	$3\,065\,91 \times 10^{-1}$	1

¹¹ Based on the values of the solar parallax and terrestrial equatorial radius laid down by the International Astronomical Union in 1964¹⁰.

Spectrometric units of length

X-Unit

$$1 \text{ XU} = [1/3029\,45\,d]_{\text{H}}^{\text{H}} (\text{CaCO}_3)$$

The very great accuracy necessary in X-ray wave-length measurements (relative uncertainty $\approx 10^{-5}$) is no longer met by SIEGBAHN'S definition of the X-unit since the natural imperfections of the calcite crystal (impurities, lattice defects, mosaic or superstructure, sur-

direct methods of other workers. In a later discussion of these

mean based on the values for constants resulting from the 1963 adjustment¹² (see page 228). Earlier, in 1965, a *special re-evaluation of the atomic constants* by COHEN and DUFOUR¹³ led to a value of $\lambda = 1\,002\,080 (3 \lambda = 18 \times 10^{-4})$ based on $\lambda(\text{WKA}) = 208\,577.0 \text{ XU}$. In 1964 BEARDEN *et al.*²¹ published the results of very precise

precision smaller than the existing tabulated values^{12, 13}, so that taking $\lambda(\text{MoK}\alpha_1) = 707\,831\,717$

gave the following mean values for the conversion factor A (relative probable error $\pm 5 \times 10^{-4}$).

$$A \approx 1\,002\,076 \text{ based on } \lambda(\text{MoK}\alpha_1) = 707\,831 \text{ XU or}$$

$$\lambda(\text{CuK}\alpha_1) = 1537\,370 \text{ XU}$$

$$\approx 1\,002\,056 \text{ based on } \lambda(\text{CuK}\alpha_1) = 1537\,400 \text{ XU or}$$

$$\lambda(\text{MoK}\alpha_1) = 707\,845 \text{ XU}$$

At the same time BEARDEN²² suggested that SIEGBAHN'S definition of the XU should be replaced by a new scale of X-ray wave lengths whose unit should be denoted provisionally by λ and de-

¹² Source authoritative¹² still use the value²¹ $1 \text{ XU} = (1\,002\,02 \pm 0.0003) \text{ m\AA}$ agreed on in 1942 between SIEGBAHN, the X-Ray Analysis Group of the Institute of Physics (UK) and the American Society for X-Ray and Electron Diffraction.

fixed by adopting an exact value of the wave length of the peak of the $W\text{K}\alpha_1$ line, namely $\lambda(W\text{K}\alpha_1) = 0.2090100 \text{ \AA}$. This defining value had been derived by BEARDEN in 1964 from the value of $\lambda(W\text{K}\alpha_1) = 208.5770 \text{ XU} = 208.5770 \times 1 \text{ m\AA}$ and his experimentally determined value $1 = 1.002076$ based on the 'working standard' wave length $\lambda(\text{MoK}\alpha_1)$; this means that the new X-ray wave-length unit also satisfies the relationship $1 \text{ m\AA} = (1.002076 \pm 5 \times 10^{-6})^{-1} \text{ XU}$. According to BEARDEN, 1 \AA is identical with 1 \AA (within a relative probable error of $\pm 5 \times 10^{-6}$).

Subsequently BEARDEN, in conjunction with six collaborators, prepared a new table²⁵ of some 2700 wave lengths of X-ray fluorescence lines of the K-, L-, M-, N- and O-series (given as maximum of the line profile) and X-ray absorption edges in his proposed \AA unit; this includes in an appendix a table of the wave lengths in XU based on $\lambda(W\text{K}\alpha_1) = 208.5770 \text{ XU}$.

In 1967 BEARDEN's wave-length table was re-published²⁶ with the following changes: 1. The new X-ray wave-length unit defined by the value $\lambda(W\text{K}\alpha_1) = 0.2090100 \text{ \AA}$ is given the symbol \AA^* [$1 \text{ \AA}^* = (1 \pm 5 \times 10^{-6}) \text{ \AA}$]. 2. As 'working standard' the wave length $\lambda(\text{CuK}\alpha_1) = 1537.400 \text{ XU}$ is given, with a resulting experimental λ value of 1.002056. 3. The wave lengths are given in \AA^* only (the appendix with values in XU is omitted). 4. The wave lengths of the 4 secondary standard lines are given in \AA^* only: $\lambda(\text{AgK}\alpha_1) = 0.5594075 \text{ \AA}^*$, $\lambda(\text{MoK}\alpha_1) = 0.709300 \text{ \AA}^*$, $\lambda(\text{CuK}\alpha_1) = 1.540562 \text{ \AA}^*$, $\lambda(\text{CrK}\alpha_1) = 2.393606 \text{ \AA}^*$ (relative probable error compared to the primary standard wave length $\lambda(W\text{K}\alpha_1) = 0.2090100 \text{ \AA}^*$: $\pm 1.1-1.3 \times 10^{-6}$).

When using BEARDEN's tables it should be noted that in the original publication²⁵ the λ value 1.002076 was based on a $\text{MoK}\alpha_1$ X-unit, i.e., it was derived from the value $\lambda(\text{MoK}\alpha_1) = 707.831 \text{ XU}$ [or $\lambda(\text{CuK}\alpha_1) = 1537.3700 \text{ XU}$ or $\lambda(W\text{K}\alpha_1) = 208.5770 \text{ XU}$], whereas in the later publication²⁶ the λ value 1.002056 is based on a 20 parts per million smaller $\text{CuK}\alpha_1$ X-unit derived from the value $\lambda(\text{CuK}\alpha_1) = 1537.400 \text{ XU}$ [or $\lambda(\text{MoK}\alpha_1) = 707.845 \text{ XU}$ or $\lambda(W\text{K}\alpha_1) = 208.5810 \text{ XU}$].

The relationship $1 \text{ \AA}^* = (1 \pm 5 \times 10^{-6}) \text{ \AA}$ given by BEARDEN for his new X-ray wave-length unit will remain valid only as long as 1. the relevant 'working standard' wave length [$\lambda(\text{MoK}\alpha_1)$ for the original tables²⁵ and $\lambda(\text{CuK}\alpha_1)$ for the later publication²⁶] and the wave-length ratios $\lambda(\text{CuK}\alpha_1)/\lambda(\text{MoK}\alpha_1) = 2.171945$ and $\lambda(\text{CuK}\alpha_1)/\lambda(W\text{K}\alpha_1) = 7.370757$ (relative probable errors $\pm 1.0 \times 10^{-6}$ and $\pm 1.1 \times 10^{-6}$) are adhered to, and 2. doubt is not thrown on the λ value (1.002076 or 1.002056) based on the relevant 'working standard' wave length by new experimental results, whether these are direct or indirect determinations of λ or new values for the atomic constants involved, in particular the Avogadro constant N_A . The second of these conditions could be avoided if, instead of introducing a new wave-length unit such as BEARDEN proposes, the now practically defunct SIEGBAHN definition of the X-unit were replaced by a new one based for instance on the $W\text{K}\alpha_1$ line: $1 \text{ XU} = \lambda(W\text{K}\alpha_1)/208.5770$ or $\lambda(W\text{K}\alpha_1)/208.5810$. Up to now the international bodies concerned have been unable to agree on a new definition of the X-unit.

Tables of the atomic energy differences (in eV and Ry; see page 213) between two levels together with the wave lengths (in \AA^*) corresponding to the energy differences are to be found in BEARDEN and BURR's tables of atomic energy levels²⁷. Some examples of energy differences are also given in the tables of energy levels published by these authors in *Reviews of Modern Physics*²⁸.

The ångström

The ångström (\AA) is widely used as a unit of length in atomic and molecular spectrometry, especially in the visible and ultraviolet spectral range. Following the new definition of the metre by the 11th General Conference on Weights and Measures¹ in 1960, the International Astronomical Union in 1961 replaced its 1907 definition²⁹ of the ångström based on the wave length of cadmium as primary standard by the relationship³⁰

$$1 \text{ ångström} = 10^{-10} \text{ metre}$$

Ångström is thus now no more than a special name for 10^{-10} m .

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Area (A or S)

Dimension = L^2

Coherent units

International System of Units: square metre (m^2)

CGS system: square centimetre (cm^2)

ft-lb-s system: square foot (ft^2)

The units of length on which the units of area are based are described on page 200.

The International Union of Pure and Applied Physics (IUPAP), at its 10th General Assembly in 1960, recommended the name barn (b) for 10^{-24} cm^2 , a quantity in common use in atomic and nuclear physics as unit of nuclear cross section¹.

Conversion of metric units of area

		1 A unit = 10 ³ B units (10 in the table)					
A		B					
Name	Symbol	μm^3	mm^3	cm^3	dm^3	m^3	km^3
barn	b	10^{-28}	10^{-33}	10^{-34}	10^{-35}	10^{-36}	10^{-39}
square micrometre ..	μm^2	1	10^{-4}	10^{-6}	10^{-10}	10^{-16}	10^{-24}
square millimetre ..	mm^2	10^4	1	10^{-2}	10^{-6}	10^{-10}	10^{-16}
square centimetre ..	cm^2	10^8	10^2	1	10^{-2}	10^{-6}	10^{-10}
square decimetre ..	dm^2	10^{12}	10^6	10^2	1	10^{-2}	10^{-6}
square metre	m^2	10^{16}	10^{10}	10^4	10^2	1	10^{-6}
square decimetre (are)	dam^2 (a)	10^{14}	10^8	10^2	10^4	10^2	10^{-6}
square hectometre (hectare)	hm^2 (ha)	10^{16}	10^{10}	10^4	10^6	10^4	10^{-6}
square kilometre ..	km^2	10^{18}	10^{12}	10^{10}	10^8	10^6	1

Conversion of Anglo-Saxon units of area

		1 A (unit) = B B units (B in the table)		
A		B		
Name	Symbol	yd ³	ft ³	m ³
circular mil*	in			
square inch	in ²			
circular inch				
square link	li***			
square foot	ft ²			
square yard	yd ²			
square rod***	rd***			
square chain	ch***			
rood (UK)	=	484	4356	4 046.86 x 10 ³
acre	=	1210	10 890	1 011.71 x 10 ³
		4840	43 560	4 046.86 x 10 ³
square mile	mile**	3 097 600	27 878 400	2 589.99 x 10 ⁴

* The circular mil is defined as the area of a circle of 0.001 inch diameter.
1 circular mil = 10^{-6} circular inch = $(\pi/4) \times 10^{-6}$ in²

* Symbols in use only in USA

*** Also known as square perch or square pole

[†] Symbol in US & mks.

Reference

Abstract

Volume (L)

Dimension = L^6

Coherent units

International System of Units cubic metre (m³)

CGS system cubic centimetre (cm³)

ft-lb system cubic foot (ft³)

The units of length on which the units of volume are based are described on page 200.

Conversion of metric units of volume

		1 A unit = 10 B units (if in this table)					
A		B					
Name	Symbol	mm ³	μm ³	mm ³	cm ³	dm ³	m ³
cubic nanometre	nm ³	1	10 ⁻⁹	10 ⁻¹²	10 ⁻²¹	10 ⁻²⁴	10 ⁻²⁷
cubic micrometre	μm ³	10 ⁹	1	10 ⁻⁶	10 ⁻¹⁵	10 ⁻¹⁸	10 ⁻²¹
cubic millimetre	mm ³	10 ¹⁸	10 ¹²	1	10 ⁻³	10 ⁻⁶	10 ⁻⁹
cubic centimetre	cm ³	10 ²⁷	10 ²¹	10 ³	1	10 ⁻³	10 ⁻⁶
cubic decimetre	dm ³	10 ³⁶	10 ³⁰	10 ⁶	10 ³	1	10 ⁻³
cubic metre (siere*)	m ³ (si)	10 ²⁷	10 ²¹	10 ³	10 ⁶	10 ⁹	1
cubic kilometre	km ³	10 ³⁶	10 ³⁰	10 ⁶	10 ⁹	10 ¹²	10 ⁹

* Name mainly in use in French-speaking countries.

* Name mainly in use in French-speaking countries.

Noncoherent unli

Up to 1964 the *litre* (l) was defined as the volume of 1 kg of pure air-free water at its maximum density ($\approx 3.98^{\circ}\text{C}$) under normal atmospheric pressure (1 atm = 760 torr)². In 1950 the International Committee of Weights and Measures³ gave 1 litre = 1,000.02 cubic decimetre (relative uncertainty $\approx \pm 3 \times 10^{-6}$) as the best conversion factor between the litre so defined and the cubic decimetre.

In 1964 the 12th General Conference of Weights and Measures

[illegible]

$\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$

types: $11 = 1 \text{ dm}^3$

Conversion of decimal submultiples and multiples of the litre

		1 A unit = 10 ³ B units (# in the table)			
A		B			
Name	Symbol	μ l	ml	l	m ³
microlitre (= 1 mm ³)	μ l	1	10 ⁻³	10 ⁻³	10 ⁻⁶
millilitre (= 1 cm ³)	ml	10 ³	1	10 ⁻³	10 ⁻⁶
decilitre (= 0.1 dm ³)	dl	10 ⁵	10 ²	10 ⁻¹	10 ⁻⁴
litre (= 1 dm ³)	l	10 ⁶	10 ³	1	10 ⁻³
hectolitre (= 0.1 m ³)	hl	10 ⁸	10 ⁵	10 ²	10 ⁻¹

Anglo-Saxon units of volume⁴

In the United Kingdom the commercial units of volume both for fluids and dry substances are the gallon (gal) and units derived from it. The gallon is the volume of a quantity of water of a specific mass when weighed under the conditions laid down⁸; this definition results in the following relationships:

$$1 \text{ gal(UK)} = 277.42 \text{ in}^3 \\ = 4\,546.09 \text{ dm}^3$$

In the United States the gallon (gal) and the units of volume derived from it are legal measures only for fluids. The gallon there defined^{6, 7} as

$$1 \text{ gal(US)} = 231 \text{ in}^3 \\ = 3.785\,411\,784 \text{ dm}^3$$

whence the relationships

1 gal(US) = 0.832674 gal(UK)

1 gal(US) = 0.832674 gal(UK)
1 gal(UK) = 1.200950 gal(US)

In the United States the units of volume for dry substances are the bushel (bu) and units derived from it. The bushel (bu) is defined as follows:

$$1 \text{ bu(US)} = 2150.42 \text{ in}^3 \\ = 35\,239.070\,166\,88 \text{ dm}^3$$

This unit is related to the bushel used in the United Kingdom defined as 1 bushel (UK) = 8 gal(UK), as follows:

1 bu(US) = 0.968939 bushel(UK)

1 bushel(UK) = 1 032 057 bu(US)

Conversion of Anglo-Saxon units of volume

A		B		
Name	Symbol	yd ³	ft ³	m ³
cubic inch	in ³	1/46 656	1/1728	1 638 706 4 × 10 ⁻⁶
cubic foot (number)	ftm ³	1/324	1/12	2 359 74 × 10 ⁻³
cubic foot	ft ³	1/27	1	2 831 68 × 10 ⁻³
cubic yard	yd ³	1	27	7 645 55 × 10 ⁻¹
cubic meter	m ³	128/27	128	3 624 56

Conversion of United Kingdom units of volume (UK units)

A		1 A unit = b B units (b in the table)		
		B		
Name	Symbol	gal	in ³	l = dm ³
minim	min	1/76 800	$3.612\ 23 \times 10^{-3}$	$5.919\ 39 \times 10^{-5}$
fluid drachm. (= 60 min)	fl dr	1/1280	$2.167\ 34 \times 10^{-1}$	$3.551\ 63 \times 10^{-3}$
fluid ounce . .	fl oz	1/160	1.733 87	$2.841\ 31 \times 10^{-2}$
(= 480 min)				
gill	–	1/32	8.669 36	$1.420\ 65 \times 10^{-1}$
pint	–	1/8	$3.467\ 74 \times 10$	$5.682\ 61 \times 10^{-1}$
quart	–	1/4	$6.935\ 49 \times 10$	1.136 52
gallon	gal	1	$2.774\ 20 \times 10^2$	4.546 09
peck	–	2	$5.548\ 39 \times 10^2$	9.092 18
bushel	–	8	$2.219\ 35 \times 10^3$	$3.636\ 87 \times 10$
quarter	–	64	$1.775\ 49 \times 10^4$	$2.909\ 50 \times 10^2$
(volume)				
chaldron	–	288	$7.989\ 68 \times 10^4$	$1.309\ 27 \times 10^3$

Conversion of United States units of volume (US units)

For fluids (liquid measure)

A		1 A unit = b B units (b in the table)		
		B		
Name	Symbol	gal	in ³	l = dm ³
minim	min	1/61 440	$3.759\ 77 \times 10^{-3}$	$6.161\ 15 \times 10^{-5}$
fluid dram . .	fl dr	1/1024	$2.255\ 86 \times 10^{-1}$	$3.696\ 69 \times 10^{-3}$
fluid ounce . .	fl oz	1/128	1.804 69	$2.957\ 35 \times 10^{-2}$
gill	gi	1/32	7.218 75	$1.182\ 94 \times 10^{-1}$
liquid pint . .	liq pt	1/8	$2.887\ 5 \times 10$	$4.731\ 76 \times 10^{-1}$
liquid quart . .	liq qt	1/4	5.775×10	$9.463\ 53 \times 10^{-1}$
gallon	gal	1	2.31×10^2	3.785 41
barrel (petroleum) ^{7,8}		42	9.702×10^3	$1.589\ 87 \times 10^2$

For dry substances (dry measure)

A		1 A unit = b B units (b in the table)		
		B		
Name	Symbol	bu	in ³	l = dm ³
dry pint	dry pt	1/64	$3.360\ 03 \times 10$	$5.506\ 10 \times 10^{-1}$
dry quart . . .	dry qt	1/32	$6.720\ 06 \times 10$	1.101 22
peck	pk	1/4	$5.376\ 05 \times 10^2$	8.809 77
bushel*	bu	1	$2.150\ 42 \times 10^3$	$3.523\ 91 \times 10$
barrel**	bbl	105/32†	7.056×10^3	$1.156\ 27 \times 10^2$

* So-called stricken or struck bushel. There is also a heaped bushel of 2747.715 in³ ≈ 45.027 l for apples and a heaped bushel = 1½ stricken bushels = 44.049 l^{6,7}.

** For fruit and other products except cranberries this barrel = 7056 in³; for cranberries the barrel = 5826 in³ ≈ 95.471 l^{6,7}.

† This fraction is an approximate. Precise calculation based on the cubic inch definitions of bushel and barrel gives 1 bbl = (7056/2150.42) bu.

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- 4 SKINNER, F. G., *Weights and Measures: Their Ancient Origins and Their Development in Great Britain up to AD 1853*, H.M.S.O., London, 1967; KAYE and LABY, *Tables of Physical and Chemical Constants and Some Mathematical Functions*, 13th ed., Longmans, London, 1966; STILLE, U., *Messen und Rechnen in der Physik*, 2nd ed., Vieweg, Braunschweig, 1961.
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- 6 United States of America, *U.S. Code of Federal Regulations*, 1946, Title 15, Ch. 6: Metric System, Sec. 204 – Metric System authorized (1866), Sec. 205 – Authorized Tables (1866), Revised Statutes, Sec. 3570; U.S. Coast and Geodetic Survey, Treasury Department, Bulletin No. 26: *Fundamental Standards*

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⁷ JUDSON, L. V., *Units of Weight and Measure (United States Customary and Metric)*, *Definitions and Tables of Equivalents*, National Bureau of Standards, Miscellaneous Publications No. 233, U.S. Government Printing Office, Washington, 1960.

⁸ International Organization for Standardization, *Basic Quantities and Units of the SI*, ISO Recommendation R 31, Part 1, 2nd ed., December 1965.

Mass (m)

Dimension = M

Coherent units

International System of Units: kilogramme (kg)

CGS system: gramme (g)

ft-lb-s system: pound (lb)

International System of Units

The base unit of mass is the kilogramme (kg)*. It is equal to the mass of the international prototype of the kilogramme, a platinum-iridium cylinder preserved at the International Bureau of Weights and Measures in Sèvres (France)¹.

Conversion of metric units of mass

A		1 A unit = b B units (b in the table)							
		B							
Name	Symbol	ag	fg	pg	ng	µg	mg	g	kg
attogramme . .	ag	1	10 ⁻³	10 ⁻⁶	10 ⁻⁹	10 ⁻¹²	10 ⁻¹⁵	10 ⁻¹⁸	10 ⁻²¹
femtogramme . .	fg	10 ³	1	10 ⁻³	10 ⁻⁶	10 ⁻⁹	10 ⁻¹²	10 ⁻¹⁵	10 ⁻¹⁸
picogramme . .	pg	10 ⁶	10 ³	1	10 ⁻³	10 ⁻⁶	10 ⁻⁹	10 ⁻¹²	10 ⁻¹⁵
nanogramme . .	ng	10 ⁹	10 ⁶	10 ³	1	10 ⁻³	10 ⁻⁶	10 ⁻⁹	10 ⁻¹²
microgramme*	µg	10 ¹²	10 ⁹	10 ⁶	10 ³	1	10 ⁻³	10 ⁻⁶	10 ⁻⁹
milligramme . .	mg	10 ¹⁵	10 ¹²	10 ⁹	10 ⁶	10 ³	1	10 ⁻³	10 ⁻⁶
gramme	g	10 ¹⁸	10 ¹⁵	10 ¹²	10 ⁹	10 ⁶	10 ³	1	10 ⁻³
kilogramme . .	kg	10 ²¹	10 ¹⁸	10 ¹⁵	10 ¹²	10 ⁹	10 ⁶	10 ³	1
metric ton (tonne)	t	10 ²⁴	10 ²¹	10 ¹⁸	10 ¹⁵	10 ¹²	10 ⁹	10 ⁶	10 ³

* Formerly also known as the gamma (γ), a name that should no longer be used.

Technical unit of mass

In the so-called 'technical system of measurement', the still widely used metre-kilopond-second system (m-kp-s system; on the kilopond see under 'Force', page 211) the coherent derived unit of mass, the so-called 'technical mass unit', is $1\text{ m}^{-1}\text{ kp s}^2 = 9.806\ 65\text{ kg}$. This unit has been little used and with the rapidly increasing popularity of the SI units it will cease to have any importance. In technology the physical quantity mass (*m*) is usually replaced by the quotient weight/acceleration due to gravity (*G/g*) (see under 'Force', page 211), the unit of which is $1\text{ kp}/9.806\ 65\text{ m s}^{-2}$, equal to the kilogramme of the MKS system.

International unit for precious stones

1 metric carat = 0.000 2 kg = 0.2 g = 200 mg²

Anglo-Saxon units of mass

In the Anglo-Saxon countries, in addition to the metric units employed in scientific work, three groups of mass units are in simultaneous use: the *avoirdupois* units of commerce and industry, the *tray* units for precious metals and coins, and the *apothecaries'* units. Common to all three groups is the grain (gr), defined as the 7000th part of the avoirdupois pound (lb avdp or lb av).

The avoirdupois pound has for some years been related³ to the kilogramme by a precise numerical factor:

1 pound (lb) = 0.453 592 37 kg

* In the USA, usually 'kilogram'.

Name	Symbol	gr	lb	kg
grain (UK, US)	gr	1	1/7000	6.479891×10^{-5}
drum (UK, US)	dr	875/32	1/256	1.77185×10^{-3}
ounce (UK, US)	oz	875/2	1/16	2.83495×10^{-2}
pound (UK, US)	lb	7×10^4	1	4.5359237×10^{-1}
stone (UK)	=	9.8×10^4	14	6.35029
quarter (UK)	qr	1.96×10^4	28	1.27006×10
cental (UK)	=	7×10^4	100	4.53592×10
short hundred-weight (US)	sh cwt			
hundredweight (UK)	cwt	7.84×10^3	112	5.08023×10
long hundred-weight (US)	=	1.4×10^7	2000	9.07185×10^3
(short) ton (US)	sh tn			
ton (UK)	ton			
long ton (US)	=	1.568×10^7	2240	1.01605×10^3

Troy units

1 A unit = B units (B in the table)				
A		B		
Name	Symbol	gr	lb	g
pennyweight	dwt	24	3/875	1.55517
troy ounce	oz t*	480	12/175	3.11035×10
troy pound (US)	lb t	5760	144/175	3.73242×10^3

* In the United States, oz t

Apothecaries' units

1 A unit = B units (B in the table)				
A		B		
Name	Symbol	gr	lb	g
scruple (UK)	s apoth*	20	1/350	1.29598
apothecaries' scruple (US)				
drachm (UK)	ds apoth*	60	3/350	3.88793
apothecaries' dram (US)				
apothecaries' ounce (UK, US)	oz apoth*	480	12/175	3.11035×10
apothecaries' pound (US)	lb apoth*	5760	144/175	3.73242×10^3

* In the United States, ap instead of apoth

References

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Time (t)

Dimension = t

Base unit: second (s)
(in all systems of measurement)

Time scales can be derived from all periodic natural phenomena (axial rotation of the earth, revolution of the planets and moon, transitions in atoms and molecules). The second of the International System of Units (SI units) is now (since October 1967) linked to an atomic frequency, it is defined as the duration of

scale derived from the axial rotation of the earth is used. For historical data on the second and on the 'atomic clock' see the literature²

Units of time derived from the earth's rotation - Universal Time

The *apparent solar day* is the time elapsing between two successive passages of the mean sun through the meridian of the observer. These passages define the time 12 noon of mean solar time (mean local time).

The mean solar day (d) is divided into 24 hours (h) each of 60 minutes (min) each of 60 seconds (s). The time taken by the mean sun to move with uniform speed along the celestial equator in such a way that its passage through the vernal equinox (one of the intersections of the celestial equator and the ecliptic) coincides with that of the true sun. The difference between apparent and mean solar time, known as the equation of time, varies in the course of the year between about +15 and -16 minutes. The mean solar day is the time elapsing between two successive passages of the mean sun through the meridian of the observer. These passages define the time 12 noon of mean solar time (mean local time).

The mean solar day (d) is divided into 24 hours (h) each of 60 minutes (min) each of 60 seconds (s).

time elapsing between two successive passages of the vernal equinox through the meridian of the observer. Since the position of the vernal equinox varies as a result, the general precision of the earth the stellar day is about 9 ms shorter. The time taken by the earth to complete a 360° revolution with respect to the fixed stars d and d* are related by

$$d = d^*(1 + 1/n)$$

where n is the number of mean solar days in the tropical year.

The stellar day (d*) is divided into 24 stellar hours (h*) each of 60 stellar minutes (min*) each of 60 stellar seconds (s*).

On the *Universal Time* scale the time 12 noon UT is defined by the passages of the mean sun through the zero meridian (Greenwich). Statutory local time scales in use in particular countries are *zonal time scales* (15° difference of longitude \approx 1 h), for example Central European Time (CET) = Universal Time + 1 h. For the differences between the various local times see the yearbooks issued by the Bureau des Longitudes².

Times on a particular time scale are often given with the symbols h, m (instead of min) and s raised, for example 2^h25^m3^s CET. In astronomy a particular point in time is known as an epoch.

Variations in the polar altitude of the earth and the seasonal variations in the earth's rotation (the latter in a pattern remaining roughly constant from year to year) result in changes in the length of the mean solar day that can be calculated. This has made it possible to define a more uniform scale of Universal Time known as UT 2. Up to 1956 the second of UT 2 was in use for very precise time measurements, but this practice has since been abandoned because the gradual slowing of the earth's rotational speed causes the second of UT 2 to increase by about 2×10^{-10} s per year. Moreover, irregular variations in the earth's rotation may result in fairly rapid changes in the UT second of, for instance, 10⁻⁸ s during the course of the year.

Multiples of the mean solar day and UT second

Calendar ordinary year = 365 mean solar days = 31 536 000 UT seconds

Calendar leap year = 366 mean solar days = 31 622 400 UT seconds

Mean Julian year (a_{jul}) = (3 calendar ordinary years + 1 calendar leap year)/4 = 365.25 mean solar days = 31 557 600 UT seconds

Mean Gregorian year (a_{greg}) = (400 a_{jul} - 3 d)/400 = 365.2425 mean solar days = 31 556 952 UT seconds

The definitions of the mean Julian and Gregorian years are chosen in such a way that their lengths approximate to that of the tropical year (ca. 365.2422 mean solar days). This figure is not constant but varies not only as a result of changes in the earth's rotation but also because the length of the tropical year itself is variable.

The zero point of the Universal Time scale is January 1 of the year 1 B.C. at 0^h UT, so that the number of the year indicates the number of complete calendar years that have since elapsed. It should be noted that only one calendar year separates 1 B.C. 0^h UT and 1 A.D. 0^h UT.

Up to 1581 each year exactly divisible by 4 was a leap year, as were the years 1, 5, 9, etc. B.C. This constituted the so-called Julian Calendar, introduced by JULIUS CAESAR in 45 B.C. Owing to the fact that the Julian year is some 11 minutes longer than the tropical year (based on the earth's orbital motion) the Julian Calendar showed earlier and earlier dates for natural events like the seasons. The growing discrepancy was finally rectified by the calendar reform introduced by POPE GREGORY XIII's bull of February 24 1582. Under this reform, 10 days were to be dropped from the calendar of the year 1582, October 5-14 inclusive, in order to restore the vernal equinox to March 21. France adopted the reform the same

year, dropping the days from December 10 to 19 1582. In England the Gregorian Calendar was not adopted until 1752, when 11 days September 3-13, had to be dropped. In order to keep the Gregorian Calendar in step with the tropical years, the reform also laid down that three out of every four century years were to be ordinary year instead of leap years, i.e., that only those century years divisible by 400 were to be leap years. The mean Gregorian year is therefore 0.4 min longer than the tropical year.

Units of time derived from the orbital movement of the earth - Ephemeris Time

The following time intervals are derived from the revolution of the earth around the sun:

The *sidereal year* (a_{sid}) is the time taken by the earth to complete one 360° revolution around the sun, as related to the system of fixed stars. Since it cannot be measured directly the sidereal year is not used in time measurements.

The *anomalous year* (a_{anom}) is the time elapsing between two successive passages of the earth through the perihelion.

The *astronomical year* (a_{astr}), also known as Bessel's year or annus fictus, is the time during which the right ascension of the (fictitious) mean sun increases by 360°; it differs only slightly from the tropical year.

The *tropical year* (a_{trop}), of great importance in time measurements, is the time elapsing between two successive passages of the true sun through the mean vernal equinox. Owing to the general precession of the earth the vernal equinox moves once round the ecliptic in about 26 000 years. In addition to this movement, the vernal equinox is subject to a slight 'secular' acceleration as well as to periodic fluctuations. The fictitious *mean* vernal equinox is not subject to these periodic fluctuations. As a result of the general precession of the earth the tropical year is 20.4 min shorter than the sidereal year, and because of the secular acceleration of the vernal equinox each tropical year is about 5.3 ms shorter than the preceding one. The tropical year remains in phase with the seasons of the earth.

In order to construct calendars the approximate tropical year up to 1581 was calculated from the mean Julian year based on the mean solar day (a_{trop} is 11.2 min shorter) and for 1583 and subsequently from the mean Gregorian year likewise based on the mean solar day (a_{trop} is 0.4 min shorter). The tropical year is also 20.4 min shorter than the sidereal year and 25.1 min shorter than the anomalous year.

The tropical year at a particular epoch is equal to $360^\circ/(dL/dt)$, where L is the mean longitude of the sun, or angle subtended at the earth by the positions of the mean sun and the mean vernal equinox at that epoch. Owing to the secular acceleration of the vernal equinox the angular velocity dL/dt is a function of time. Of special importance is the length of the tropical year at the epoch 1900, January 0, 12 noon Ephemeris Time, which is December 31

Conversion of units of time

		1 A unit = b B units (b in the table)						
		A (Universal Time)		B (Universal Time)				
				s	min	h	d	Symbol
Name		Symbol						
Mean solar time	second	s	1	1.6×10^{-2}	2.7×10^{-4}	$1.157\,40 \times 10^{-5}$	s	
	minute	min	6×10	1	1.6×10^{-2}	6.94×10^{-4}	min	
	hour	h	3.6×10^3	6×10	1	4.16×10^{-2}	h	
	day	d	8.64×10^4	1.44×10^3	2.4×10	1	d	
	month {	28 days		$2.419\,2 \times 10^6$	4.032×10^4	6.72×10^2	2.8×10	month {
		29 days		$2.505\,6 \times 10^6$	4.176×10^4	6.96×10^2	2.9×10	
		30 days		2.592×10^6	4.32×10^4	7.2×10^2	3×10	
		31 days		$2.678\,4 \times 10^6$	4.464×10^4	7.44×10^2	3.1×10	
	year {	365 days	a_{365}	$3.153\,6 \times 10^7$	5.256×10^5	8.76×10^3	3.65×10^2	a_{365}
		366 days	a_{366}	$3.162\,24 \times 10^7$	$5.270\,4 \times 10^5$	8.784×10^3	3.66×10^2	
Stellar time	stellar second ^B	s*	$9.972\,696 \times 10^{-1}$	$1.662\,116 \times 10^{-2}$	$2.770\,193 \times 10^{-4}$	$1.154\,247 \times 10^{-5}$	s*	
	stellar minute ^B	min*	$5.983\,617 \times 10$	$9.972\,696 \times 10^{-1}$	$1.662\,116 \times 10^{-2}$	$6.925\,483 \times 10^{-4}$	min*	
	stellar hour ^B	h*	$3.590\,170 \times 10^3$	$5.983\,617 \times 10$	$9.972\,696 \times 10^{-1}$	$4.155\,290 \times 10^{-2}$	h*	
	stellar day ^B	d*	$8.616\,409 \times 10^4$	$1.436\,068 \times 10^3$	$2.393\,447 \times 10$	$9.972\,696 \times 10^{-1}$	d*	
Cal-endar years	julian year	a_{jul}	$3.155\,76 \times 10^7$	$5.259\,6 \times 10^5$	8.766×10^3	$3.652\,5 \times 10^2$	a_{jul}	
	gregorian year	a_{greg}	$3.155\,695\,2 \times 10^7$	$5.259\,492 \times 10^5$	$8.765\,82 \times 10^3$	$3.652\,425 \times 10^2$	a_{greg}	
A (Ephemeris Time)		B (Ephemeris Time)						
At time 1900.0	sidereal year ^B	a_{sid}	$3.155\,814\,97 \times 10^7$	$5.259\,691\,62 \times 10^5$	$8.766\,152\,71 \times 10^3$	$3.652\,563\,83 \times 10^2$	a_{sid}	
	tropical year ^B	a_{trop}	$3.155\,692\,60 \times 10^7$	$5.259\,487\,66 \times 10^5$	$8.765\,812\,77 \times 10^3$	$3.652\,421\,99 \times 10^2$	a_{trop}	
	anomalous year ^B	a_{anom}	$3.155\,843\,30 \times 10^7$	$5.259\,738\,83 \times 10^5$	$8.766\,231\,38 \times 10^3$	$3.652\,596\,41 \times 10^2$	a_{anom}	

899, 12 noon plus $\approx 4.5^s$ Universal Time. At this time the mean

moon's orbital and the earth's axial rotational frequencies is well known.

mean solar day (i.e., seconds of Universal Time) at the time 1900 0. This is, however, incorrect. The mean day is Newcomb's calculated mean value of the mean solar day during the period 1680-1895.

Units of time derived from atomic transitions - Atomic Time

Atomic Time is based on the frequencies corresponding to hyperfine structure transitions in the atoms of the caesium, hydrogen and thallium nuclides ^{133}Cs , ^1H and ^{205}Tl , in the classical interpretation such transitions are due to the precession of the electrons of the nucleus spin (hyperfine structure) in the magnetic field of the

periods of the atomic frequencies must be counted continuously. A typical instrument for this purpose is variously known as a caesium beam apparatus, caesium atomic clock or caesium time and frequency standard.

Since the ephemeris second is known only to an accuracy of 10^{-9} s and is thus inadequate for precise time and frequency measurements the time unit is defined as the duration of 9192631770 periods of the radiation corresponding to the transition between the two hyperfine levels of the ground state of the ^{133}Cs atom. The 13th General Conference of Weights and Measures, in October 1967 adopted this relationship as the basis for the new definition of the SI second, and the ephemeris second continues to be used only in astronomy.

Standard frequency and time-signal transmitters transmit time signals by various systems. Thus UTC (Coordinated Universal Time) signals are transmitted partly with the aid of a time scale derived from atomic clocks that agrees approximately with Universal Time 2 and remains unchanged in each case for one calendar year. When the deviation from Universal Time exceeds 0.1s the UTC signals are readjusted. Other transmitters send out SAT (Stepped Atomic Time) signals whose time unit is the atomic second. Here too the time signals are adjusted only when the deviation from Universal Time exceeds 0.1s.

References

- ¹ Conférence Générale des Poids et Mesures, *Compte rendu des 13^e Conférence générale des Poids et Mesures*, Paris 1967/1968, Bureau International des Poids et Mesures, Prot.-Verb. Com. Int. P 25, 77 (1957).
- ² Conférence Générale des Poids et Mesures, *Compte rendu des 11^e Conférence générale des Poids et Mesures*, Paris 1960, Gauthier-Villars 1961, page 86.
- ³ Nicholson and Sadler, *Nature*, 210, 187 (1966).
- ⁴ Conférence Générale des Poids et Mesures, *Compte rendu des 12^e Conférence générale des Poids et Mesures*, Paris 1964, Gauthier-Villars 1964, page 93.
- ⁵ Values from or calculated from Bureau des Longitudes, *Annuaire* 1966, Gauthier-Villars, Paris, 1965.

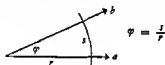
Angle ($\alpha, \beta, \gamma, \theta, \varphi$)

Dimension = L^0

Plane angles

SI unit: radian (rad) $\approx 1/\text{m}$

The plane angle φ between two straight lines a and b is as the ratio of the arc s to the radius r of a circle whose centre is at the point of intersection of the lines.



Since the angle φ is the ratio of two lengths it is a dimensionless quantity.

Plane angles

1 degree ($^\circ$) = 60 minutes ($'$) = 60×60 seconds ($''$)

The grade is subdivided centesimally.

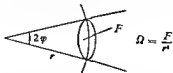
1 grade (g) = 100 centesimal minutes (m) = 100×100 centesimal seconds (s)

The radian, right angle and whole circular angle are subdimensionally without special designation.

Solid angles (Ω)

SI unit: steradian (sr) = $1/\text{m}^2$

The solid angle Ω is defined as the ratio F/r^2 , where F is the area of the surface of a sphere of radius r cut out by a cone whose vertex is at the centre of the sphere.



Since the solid angle is the ratio of two areas it is a dimensionless quantity. When the spatial angle of the cone is small the following relation holds:

$$\Omega \approx 2\pi(1 - \cos \varphi)$$

The steradian (sr) is defined as the solid angle subtending the surface of a sphere of unit radius by a cap of unit area on the surface of the sphere. The square degree [symbol: $^\circ$ or $(^\circ)^2$] is defined as $(\pi/180)^2$ sr, the square grade [symbol: g] by $(\pi/200)^2$ sr.

Conversion of plane angles

		1 A unit = b B units (b in the table)		
A		B		
Name	Symbol	°	′	rad
degree	°	1	1.1	$1.745\,328 \times 10^{-2}$
minute	′	1.6×10^{-2}	$1.851\,85 \times 10^{-2}$	$2.908\,882 \times 10^{-4}$
second	″	2.7×10^{-4}	$3.086\,420 \times 10^{-4}$	$4.848\,137 \times 10^{-6}$
grade	g	9×10^{-1}	1	$1.570\,796 \times 10^{-2}$
centesimal minute ...	°	9×10^{-3}	10^{-2}	$1.570\,796 \times 10^{-4}$
centesimal second ...	co	9×10^{-5}	10^{-4}	$1.570\,796 \times 10^{-6}$
radian	rad	$5.729\,579 \times 10^1$	$6.366\,198 \times 10^1$	1
right angle ...	L	9×10^1	10^2	$1.570\,796$
whole	2π rad	3.6×10^2	4×10^2	$6.283\,185$

Conversion of solid angles

		1 A unit = b B units (b in the table)		
A		B		
Name	Symbol	□°	(°)²	sr
square degree ..	□°	1	1.234 568	$3.046\,174 \times 10^{-4}$
square grade ...	(g)²	8.1×10^{-1}	1	$2.467\,401 \times 10^{-4}$
steradian	sr	$3.282\,806 \times 10^3$	$4.052\,847 \times 10^3$	1

Frequency (ν or $f = 1/T$; T = period)Dimension = T^{-1} SI unit: hertz (Hz) = 1 s^{-1}

In Anglo-Saxon usage the reciprocal second as frequency unit is sometimes designated cycle per second (c/s), often wrongly shortened to cycle (c). 1 kilohertz (kHz; kilocycle per second, kc/s) = 1000 Hz.

Angular frequency (pulsatance) $\omega = 2\pi f$ should not be expressed in hertz (Hz) but in reciprocal seconds (s^{-1}). 1 reciprocal millisecond (ms^{-1}) = 1000 s^{-1} .

Frequency of rotation (n)Dimension = T^{-1} SI unit: reciprocal second (s^{-1})

Other units

Revolution/second (r s^{-1}) = 1 s^{-1} ; revolution/minute (r min^{-1}) = $1.6 \times 10^{-2}\text{ s}^{-1}$; revolution/hour (r h^{-1}) = $2.7 \times 10^{-4}\text{ s}^{-1}$; revolution/day (r d^{-1}) = $1.5740 \times 10^{-5}\text{ s}^{-1}$

Temperature

Dimension = θ

The concepts *temperature* and *heat* (quantity of heat) are rigorously differentiated in physics. The same quantity of heat can be distributed over a larger or smaller amount of the same material, which will have a lower temperature in the former case than in the latter.

Heat is a form of energy (see 'Energy', page 212), while the temperature of a body is a measure of the average kinetic energy per degree of freedom of the constituent molecules. Since it is related to the average movement of the latter, the concept of temperature can be applied only to bodies consisting of a large number of molecules. This simple relationship no longer applies at very low temperatures.

Thermodynamic temperature (T) and temperature scales

The only term for temperature that allows clear and consistent expression of all the states, processes and laws of thermodynamics is the thermodynamic temperature T , whether this is introduced by way of relationships between quantities of classical thermodynamics (for instance, the amounts of heat and work in a CARNOT cycle or the behaviour of ideal gases) or statistically defined (either

kinetically, starting from the energy distribution of the molecules of a system or from the characteristic parameter $\theta = kT$ of the GIBBS canonical distribution in statistical mechanics)¹. In a CARNOT cycle operating between two temperatures T_1 and $T_2 < T_1$ the amounts of heat Q_1 and Q_2 absorbed or liberated are proportional to the corresponding temperatures: $Q_1/Q_2 = T_1/T_2$. According to the Second Law of Thermodynamics the thermodynamic temperature T has a lowest value below which it cannot fall and which can be given the value zero: the 'absolute zero' of thermodynamics. In a CARNOT cycle operating between a finite temperature T_1 and the absolute zero (a special case in physics) the efficiency (η = work done, ΔA , divided by the amount of heat removed, ΔQ) attains the value 1.

International System of Units

The base unit of thermodynamic temperature is the kelvin (K), defined^{2,3} as the fraction $1/273.16$ of the thermodynamic temperature T_{tr} of the triple point of water (the point at which the solid, liquid and gaseous phases of pure water are in equilibrium). The same name kelvin (K) is also used to express an interval or a difference of thermodynamic temperature $\Delta T = T_1 - T_2$.*

This definition is also the basis of the thermodynamic Kelvin scale, starting at the absolute zero $T = 0\text{ K}$, introduced by Lord KELVIN in 1848; as a linear scale this can be constructed from any variable quantity bearing a linear relationship to the thermodynamic temperature T . Such a simple relationship relates the energy of ideal gases to a function of temperature expressed by the equation of state $T = pV_{mo}/R$ (where p = gas pressure, V_{mo} = molar volume of an ideal gas, R = molar gas constant (see under 'Physical Constants', page 228) and can be determined experimentally by means of a gas thermometer.

Anglo-Saxon unit of thermodynamic temperature

Also occasionally used as unit of thermodynamic temperature is the degree Rankine (°R), defined as $5/9$ of the kelvin⁴. The thermodynamic Rankine scale starts at the absolute zero $T = 0\text{ °R}$, and can likewise be realized by gas thermometry.

When expressing temperature interval $\Delta T = T_1 - T_2$ the degree Rankine is usually written degR.

Celsius temperature (t) and temperature scale

The Celsius temperature t assigned to a system is defined as the difference between the corresponding thermodynamic temperature T of the system and a special thermodynamic temperature $T_{0,c}$ the value of which has no special physical significance but is arbitrarily chosen and conventionally fixed^{4,5,*}: $t = T - T_{0,c}$. The zero point defining Celsius temperature is the temperature $T_{0,c} = 273.15\text{ K}$ lying 0.01 K below the triple point of water.

To express Celsius temperatures the base SI unit kelvin is designated simply degree Celsius (°C). The thermodynamic Celsius scale is subdivided into the same intervals as the thermodynamic Kelvin scale but has a zero point displaced by 273.15 K. The Celsius temperature $t_0 = 0\text{ °C}$ expresses the same temperature as the thermodynamic temperature $T_{0,c} = 273.15\text{ K}$. The degree Celsius (°C) or the kelvin (K), as names and symbols for the same unit, may be used to express an interval or a difference of Celsius temperature $\Delta t = t_1 - t_2$ equal to an interval or difference of thermodynamic temperature $\Delta T = T_1 - T_2$.

Fahrenheit temperature (θ) and temperature scale

In English-speaking countries Fahrenheit temperature θ also continues in use for the time being. The Fahrenheit temperature assigned to a system is defined as the difference between the corresponding thermodynamic temperature T of the system and a special temperature $T_{0,F}$ established by convention and without special physical significance⁴: $\theta = T - T_{0,F}$. The zero point defining Fahrenheit temperature is the temperature $T_{0,F} = 459.67\text{ °R}$ lying 32.018 °R below the triple point of water.

To express Fahrenheit temperatures the degree Rankine is designated simply degree Fahrenheit (°F). The thermodynamic Fahrenheit scale is subdivided into the same intervals as the thermodynamic Rankine scale but has a zero point displaced by 459.67 degR. The Fahrenheit temperature $\theta_0 = 0\text{ °F}$ expresses the same temperature as the thermodynamic temperature $T_{0,F} = 459.67\text{ °R}$.

* The 13th General Conference of Weights and Measures³ in October 1967 abrogated the names and symbols previously used - including the degree Kelvin (°K) and degree (deg. for temperature interval or difference) - but agreed that the formulations resulting from the earlier usage should be admitted for the time being. In this chapter on 'Units of Measurement' the text conforms with the new definition of the kelvin (K) but in other chapters of these *Scientific Tables* the old usage is followed.

When expressing a temperature interval or difference $\Delta\theta = t_1 - t_2$ the degree Fahrenheit is usually written degF ($= \text{degR}$)

Conversion of temperature units and values

(a) Between temperature interval units—

$$1 \text{ degR} = 1 \text{ degF} = \frac{5}{9} \text{ K} = \frac{5}{9} ^\circ\text{C}$$

$$1 \text{ K} = 1 ^\circ\text{C} = \frac{9}{5} \text{ degR} = \frac{9}{5} \text{ degF}$$

(b) For temperature values on the four thermodynamic scales ($T = T_K = T_R^\circ\text{R}; t = t_C^\circ\text{C}, \theta = \theta_F^\circ\text{F}$).

$$T_K = \frac{5}{9} T_R = t_C + 273.15 = \frac{5}{9} (\theta_F + 459.67)$$

$$T_K = \frac{5}{9} T_R = \theta_F + 459.67 = \frac{5}{9} t_C + 491.67$$

$$t_C = T_K - 273.15 = \frac{5}{9} (T_K - 491.67) = \frac{5}{9} (\theta_F - 32)$$

$$\theta_F = T_K - 459.67 = \frac{9}{5} T_K - 459.67 = \frac{9}{5} t_C + 32$$

Fundamental points of the thermodynamic temperature scales

Unit	Symbol	Temperature value at	
		absolute zero	triple point of water*
kelvin	K	0	273.15
degree Celsius	$^\circ\text{C}$	-273.15	0.01
degree Rankine	$^\circ\text{R}$	0	491.68
degree Fahrenheit	$^\circ\text{F}$	-459.67	32.018

* Temperature at which the solid, liquid and gaseous phases of water are in equilibrium.

point of water and the absolute zero, which is very near to the old definition, means that the temperatures of the ice and steam point are now values that must be determined experimentally

International Practical Temperature Scale of 1968 (IPTS-68)

The IPTS-68 is based on the assigned values of the temperatures (columns 2 and 3 of the table below) of a number of reproducible equilibrium states (defining fixed points, column 1 of the table) and on standard instruments calibrated at these temperatures. Interpolation between the fixed point temperatures is effected by means of

the case of t and T

The defining fixed points are established by realizing specified equilibrium states between phases of pure substances. The standard instruments and interpolation formulae are as follows: in the range $13.81 \text{ K} \leq T_{90} \leq 730.89 \text{ K}$ (freezing point of antimony as a secondary reference point) the platinum resistance thermometer, in the range $730.89 \text{ K} \leq T_{90} \leq 1337.58 \text{ K}$ the platinum-10% rhodium/platinum thermocouple, in the range above 1337.58 K the PLANCK law for radiation in terms of spectral concentration of radiance L_{λ} (see page 222), with 1337.58 K as reference temperature and the value 0.014389 mK for the 2nd PLANCK radiation constant b_2 (see page 228).

The IPTS-68 has been chosen in such a way that temperature measured on it closely approximates to thermodynamic temperature $T_{90} = T + \Delta T_{90} \approx T$ and $t_{90} = t + \Delta t_{90} \approx t$. The difference is within the present limits of accuracy of measurement (see column 4 of the table). At the triple point of water both temperature values are exactly equal by definition.

Defining fixed points of the IPTS-68, values assigned to T_{90} and t_{90} , and estimated uncertainties $\Delta T_{90} = \Delta t_{90}$

Defining fixed point (equilibrium state)*	Assigned value T_{90} in K	t_{90} in $^\circ\text{C}$	$\Delta T_{90} = \Delta t_{90}$
Triple point of equilibrium hydrogen	13.81	-259.34	$\pm 0.01 \text{ K}$
25/76 standard atmosphere point of equilibrium hydrogen	17.042	-256.108	$\pm 0.01 \text{ K}$
Boiling point of equilibrium hydrogen	20.28	-252.87	$\pm 0.01 \text{ K}$
Boiling point of neon	27.102	-246.048	$\pm 0.01 \text{ K}$
Triple point of oxygen	54.361	-218.789	$\pm 0.01 \text{ K}$
Boiling point of oxygen	90.188	-182.962	$\pm 0.01 \text{ K}$
Triple point of water***	273.15	0.01 (exact by definition)	
Boiling point of water***	373.15	100	$\pm 0.005 \text{ K}$
Freezing point of zinc	692.73	419.58	$\pm 0.03 \text{ K}$
Freezing point of silver	1235.08	961.93	$\pm 0.2 \text{ K}$
Freezing point of gold	1337.58	1064.43	$\pm 0.2 \text{ K}$

alternative to the boiling point of water
*** The water used should have the isotopic composition of ocean water

Practical scales of temperature (outside the IPTS-68 range) for use over the range 0.2 K – 5.2 K

Temperatures can be derived from measured vapour pressures of ^4He and ^3He . The upper limits for use are set by the critical points of the gases (5.2 K for ^4He and 3.3 K for ^3He) and the lower limits by the minimum vapour pressure capable of practical measurement. On these scales – the '1958 ^4He Scale' and the '1962 ^3He Scale' –

vapour pressures versus temperature⁶. The '1962 ^3He Scale', re-

References

- 1 Cf. De Boer, J., *Metallography*, 1, 158 (1963)
- 2 Conférence Générale des Poids et Mesures, *Comptes rendus des séances de la 10^e Conférence générale des Poids et Mesures*, Paris 1954, Gauthier-Villars, Paris, 1955, page 79
- 3 Conférence Générale des Poids et Mesures, *Comptes rendus des séances de la 13^e Conférence générale des Poids et Mesures*, Paris 1967/1968, Bureau International des Poids et Mesures, Sevres, 1969. Résolutions 3, 4 and 8, pages 18, 19, 60

Density ($\rho = m/V$)

Dimension = L^{-3}M

Coherent units

International System of Units kilogramme/cubic metre (kg m^{-3})
CGS system gramme/cubic centimetre (g cm^{-3})
ft-lb-s system pound per cubic foot (lb ft^{-3})

The density (ρ) of a substance is the ratio of its mass to its volume. Density is dependent on both temperature and pressure.

Important density constants are the maximum density of air-free water¹ at 760 torr (i.e., at $\approx 4^\circ\text{C}$): $\rho_{\text{max}}(\text{H}_2\text{O}) = 0.999972 \text{ kg dm}^{-3}$ and the standard density of mercury: $\rho_{\text{H}}(\text{Hg}) = 13.59508 \text{ kg dm}^{-3}$.

The product of the density ρ and the (local) acceleration due to gravity g is the specific weight ($\gamma = \rho g$) of the substance. Specific weight is thus dependent not only on thermodynamic variables but also on the acceleration due to gravity, so that unlike density it is not in fact a *specific* property of a substance.

The *relative density* (d) of a substance is the ratio of its density to that of a reference substance. As the ratio of two quantities with the same dimensions it is a dimensionless quantity. Relative density is still often given the name 'specific gravity', but this is a term open to the same objection as specific weight. The usual reference density for liquids and solids is the maximum density of water, for gases the standard density of dry air free of carbon dioxide ($\rho_{\text{a}} = 1.2928 \times 10^{-3} \text{ kg dm}^{-3}$).

Since the maximum density of water is very nearly equal to 1 kg dm^{-3} relative, density in practice can usually be equated numerically with density expressed in kg dm^{-3} . Since relative density is the ratio of two densities, two particular temperatures must be specified. Thus the relative density of a substance at $20^\circ\text{C}/4^\circ\text{C}$ is the ratio

$$\frac{\text{density of the substance at } 20^\circ\text{C}}{\text{density of water at } 4^\circ\text{C}}$$

written as d^{20}_4 .

Conversion of metric units of density

A		1 A unit = b B units (b in the table)	
Name	Symbol	B	
		mg mm^{-3} g cm^{-3} kg dm^{-3}	mg cm^{-3} g dm^{-3} kg m^{-3}
microgramme per cubic centimetre	$\mu\text{g cm}^{-3}$	10 ⁻⁶	10 ⁻³
or millilitre	$\mu\text{g ml}^{-1}$		
milligramme per cubic decimetre	mg dm^{-3}		
or litre	mg l^{-1}	10 ⁻³	1
milligramme per cubic centimetre	mg cm^{-3}		
or millilitre	mg ml^{-1}		
gramme per cubic decimetre	g dm^{-3}		
or litre	g l^{-1}	1	10 ³
kilogramme per cubic metre ..	kg m^{-3}		
picogramme per cubic micrometre	$\text{pg } \mu\text{m}^{-3}$		
milligramme per cubic millimetre	mg mm^{-3}		
or microlitre	$\text{mg } \mu\text{l}^{-1}$	1	10 ³
gramme per cubic centimetre	g cm^{-3}		
or millilitre	g ml^{-1}		
kilogramme per cubic decimetre	kg dm^{-3}	1	10 ³
or litre	kg l^{-1}		

Conversion of Anglo-Saxon units of density

A		1 A unit = b B units (b in the table)	
Name	Symbol	B	
		lb ft^{-3}	kg m^{-3}
pound per cubic foot ..	lb ft^{-3}	1	1.60185×10
pound per gallon (UK) ..	lb gal(UK)^{-1}	6.228 83	9.97764×10
pound per gallon (US) ..	lb gal(US)^{-1}	1728/231	1.19826×10^2

References

- Comité International des Poids et Mesures, *Proc.-Verb. Com. int. Poids Mes.* (2), 22, 77 (1950); STILLE, U., *Messen und Rechnen in der Physik*, 2nd ed., Vieweg, Braunschweig, 1961, page 286.
- COOK and STONE, *Phil. Trans. Roy. Soc.*, 250A, 279 (1957); COOK, A. H., *Phil. Trans. Roy. Soc.*, 254A, 125 (1961); BEATTIE et al., *Proc. Amer. Acad. Arts Sci.*, 74, 371 (1941).
- OTTO and THOMAS, in HAUSEN, H. (Ed.), *Landolt-Börnstein, Physikalisch-chemische Tabellen*, 6th ed., vol. 4, part 4, section 2, Springer, Berlin, 1967, page 174; DIN, F., *Thermodynamic Functions of Gases*, vol. 2, Butterworth, London, 1956.

Linear velocity (u or $v = ds/dt$; s = distance)

Dimension = LT^{-1}

Coherent units

International System of Units: metre per second (m s^{-1})

CGS system: centimetre per second (cm s^{-1})

ft-lb-s system: foot per second (ft s^{-1})

Conversion of metric units of velocity

A		1 A unit = b B units (b in the table)		
Name	Symbol	B		
		m min^{-1}	km h^{-1}	m s^{-1}
centimetre per second	cm s^{-1}	6×10^{-1}	3.6×10^{-2}	10^{-2}
metre per minute	m min^{-1}	1	6×10^{-2}	1.6×10^{-2}
kilometre per hour	km h^{-1}	1.6×10	1	2.7×10^{-1}
metre per second	m s^{-1}	6×10	3.6	1
kilometre per second	km s^{-1}	6×10^3	3.6×10^3	10^3

Conversion of Anglo-Saxon units of velocity

A		1 A unit = b B units (b in the table)		
Name	Symbol	B		
		ft s^{-1}	mile h^{-1}	m s^{-1}
foot per minute ..	ft min^{-1}	1.6×10^{-2}	1.136×10^{-2}	5.08×10^{-3}
foot per second ..	ft s^{-1}	1	6.81×10^{-1}	3.048×10^{-1}
mile per hour ..	mile h^{-1}	1.46	1	4.4704×10^{-1}
knot	kn	1.687 81	1.150 78	5.14×10^{-1}
nautical mile per hour	n mile/h			
knot (UK)	kn (UK)	1.688 89	1.15	5.14772×10^{-1}
nautical mile (UK)	n mile (UK)			
per hour	(UK)/h	5.28×10^3	3.6×10^3	1.609344×10^3
mile per second ..	mile s^{-1}			

Angular velocity ($\omega = d\phi/dt$)

Dimension = $\text{L}^0 \text{T}^{-1}$

SI unit: radian per second (rad s^{-1})

Conversion of units of angular velocity

A		1 A unit = b B units (b in the table)		
Name	Symbol	B		
		$^\circ \text{s}^{-1}$	$^\circ \text{s}^{-1}$	rad s^{-1}
grade per minute ..	$^\circ \text{min}^{-1}$	1.6×10^{-2}	1.5×10^{-2}	2.61799×10^{-4}
degree per minute ..	$^\circ \text{min}^{-1}$	1.851×10^{-2}	1.6×10^{-2}	2.90888×10^{-4}
grade per second ..	$^\circ \text{s}^{-1}$	1	9×10^{-1}	1.57080×10^{-1}
radian per minute ..	rad min^{-1}	1.061 03	9.54930×10^{-1}	1.6×10^{-2}
degree per second ..	$^\circ \text{s}^{-1}$	1.1	1	1.74533×10^{-2}
radian per second ..	rad s^{-1}	6.36620×10	5.72958×10	1

Acceleration ($a = dv/dt$)

Dimension = LT^{-2}

Coherent units

International System of Units: metre per second squared (m s^{-2})

CGS system: centimetre per second squared (cm s^{-2})

= galileo (Gal) (for acceleration due to gravity)

ft-lb-s system: foot per second squared (ft s^{-2})

The internationally accepted value¹ of the normal acceleration due to gravity (see also page 230) is

$$g_n = 9\,806\,65\text{ m s}^{-2} = 980\,665\text{ Gal (cm s}^{-2}\text{)} \\ \approx 32\,174\,05\text{ ft s}^{-2}$$

Conversion of metric units of acceleration

		1 A unit = B units (B in the table)		
A		B		
Name	Symbol	Gal cm s ⁻²	km h ⁻¹ s ⁻¹	m s ⁻²
galileo	Gal	1	3.6×10^{-3}	10^{-3}
centimetre per second squared	cm s ⁻²			
kilometre per hour per second	km h ⁻¹ s ⁻¹			
metre per second squared	m s ⁻²	10^3	3.6	1

Conversion of Anglo-Saxon units of acceleration

		1 A unit = B units (B in the table)		
A		B		
Name	Symbol	ft s ⁻²	mile h ⁻¹ s ⁻¹	m s ⁻²
foot per second squared	ft s ⁻²	1	6.81×10^{-1}	3.048×10^{-2}
mile per hour per second	mile h ⁻¹ s ⁻¹	1.48	1	4.4704×10^{-1}

Reference

¹ Conférence Générale des Poids et Mesures, *Comptes rendus des séances de la 3^e Conférence générale des Poids et Mesures*, Paris 1901, Gauthier-Villars, Paris, 1901, page 70

Force (F) (= mass × acceleration)

Dimension = LMT⁻²

Coherent units

International System of Units: newton (N) = m kg s⁻² = 10³ dyn
CGS system: dyne (dyn) = em g s⁻² = 10⁻⁵ N
ft-lb-s system: poundal (pdl) = ft lb s⁻² = 0.138254954376 N

Conversion of noncoherent units of force (g_n = standard acceleration due to gravity = 9 806 65 m s⁻² = 32 174 048 ft s⁻²)

			1 A unit = B units (B in the table)	
A			B	
Name	Symbol	Definition	pdl	N
grain-force	grf	$g_n \times (1\text{ gr})$	4.59629×10^{-8}	6.35460×10^{-4}
pound	p			
gramme force	gf			
pound-force	lbf	$g_n \times (1\text{ lb})$	3.21740×10	4 448.22
kilopond	kp	$g_n \times (1\text{ kg})$	7.09316×10	9 806.65
kilogramme force	kpf			
short ton force	sh tonf			
ton force (UK)	tonf	$g_n \times (1\text{ sh ton})$	6.43481×10^4	8.89644×10^3
long ton force (US)	tonf	$g_n \times (1\text{ ton})$	7.20699×10^4	9.96402×10^3

Pressure (p) (= force/area)

Dimension = L⁻¹ MT⁻²

Coherent units

International System of Units: newton per square metre (N m⁻²)
= m⁻¹ kg s⁻² = 10 dyn cm⁻²
CGS system: dyne per square centimetre (dyn cm⁻²) = cm⁻¹ g s⁻²
= 0.1 N m⁻²
ft-lb-s system: poundal per square foot (pdl ft⁻²) = ft⁻¹ lb s⁻² = 6
1 489 163 943 N m⁻²

Noncoherent 'technical' units of force

In technology many units of force are still in use in which the mass unit (kilogramme, pound, etc.) is multiplied not by the coherent unit of acceleration (1 m s⁻², 1 ft s⁻², etc.) but by the standard

will in due course cease to be used. In scientific work they should in any case be avoided. In some countries, particularly France, they are no longer statutory units.

Reference

¹ Deutscher Normenausschuß, *Maß, Gewicht, Gewichtskraft, Fallbeschleunigung*, Begriffe, DIN 1305, June 1968, Beuth Verlag, Berlin, 1968

Angular acceleration ($\alpha = d\omega/dt = d^2\theta/dt^2$)

Dimension = L² T⁻²

SI unit: radian per second squared (rad s⁻²)

Conversion of units of angular acceleration

		1 A unit = B units (B in the table)		
A		B		
Name	Symbol	s s ⁻²	° s ⁻²	rad s ⁻²
grade per second squared	° s ⁻²	1	9×10^{-5}	1.57080×10^{-4}
degree per second squared	° s ⁻²	1	1	1.74533×10^{-2}
radian per second squared	rad s ⁻²	6.36620×10	5.72958×10	1

Noncoherent metric units of pressure

The 10⁵ multiple of the dyn cm⁻² is known as the *bar* (bar).

1 bar = 10⁵ millibar (mbar) = 10⁵ N m⁻² = 10⁵ dyn cm⁻²
= 10² microbar (μbar)

The millibar is now the internationally accepted unit of pressure in meteorology¹, the microbar is used in acoustics for sound pressure data.

¹ In meteorology the millibar is widely, but wrongly, denoted by the symbol mb, the recognised symbol for millibarn (see page 202).

Conversion of metric units of pressure

		1 A unit = b B units (b in the table)			
A		B			
Name	Symbol	dyn cm ⁻² = μbar	N m ⁻²	mbar	bar
dyne per square centimetre.....	dyn cm ⁻²	1	10 ⁻¹	10 ⁻³	10 ⁻⁶
microbar.....	μbar				
newton per square metre.....	N m ⁻²	10	1	10 ⁻²	10 ⁻⁶
millibar.....	mbar	10 ³	10 ²	1	10 ⁻³
bar.....	bar	10 ⁶	10 ⁵	10 ³	1

Noncoherent 'technical' units of pressure

These are derived from the 'technical' units of force and the units of area. The *technical atmosphere* (at) is widely used:

$$\begin{aligned}
 1 \text{ at} &= 10^4 \text{ kilopond/square metre (kp m}^{-2}\text{)} \\
 &= 1 \text{ kilopond/square centimetre (kp cm}^{-2}\text{)} \\
 &= 9.80665 \times 10^4 \text{ N m}^{-2} = \frac{9.80665 \times 10^4}{1.01325 \times 10^5} \text{ atm} \\
 &= 0.967841105 \text{ atm}
 \end{aligned}$$

Noncoherent special units of pressure

Standard physical atmosphere (atm). Defined in connection with the International Practical Scale of Temperature of 1948¹ as

$$1 \text{ atm} = 101325 \text{ N m}^{-2} = 1013250 \text{ dyn cm}^{-2}$$

Torr (torr). Defined as

$$1 \text{ torr} = 1 \text{ atm}/760 = 133.322368 \text{ N m}^{-2} = 1333.22368 \text{ dyn cm}^{-2}$$

*Millimetre of water** (mm water). Defined as the pressure exerted by a column of water 1 mm in height at its maximum density (0.999972 g cm⁻³) at standard pressure (760 torr) under the standard acceleration due to gravity g_n :

$$\begin{aligned}
 1 \text{ mm water} &= 0.1 \text{ cm} \times 0.999972 \text{ g cm}^{-3} \times 980.665 \text{ cm s}^{-2} \\
 &= 9.80637541 \text{ N m}^{-2} = 98.0637541 \text{ dyn cm}^{-2}
 \end{aligned}$$

*Conventional millimetre of water** (mmH₂O). Defined as the pressure exerted by a column of liquid 1 mm in height with a density of 1 g cm⁻³ under the standard acceleration due to gravity g_n :

$$\begin{aligned}
 1 \text{ mmH}_2\text{O} &= 0.1 \text{ cm} \times 1 \text{ g cm}^{-3} \times 980.665 \text{ cm s}^{-2} \\
 &= 9.80665 \text{ N m}^{-2} = 98.0665 \text{ dyn cm}^{-2} = 1 \text{ kp m}^{-2}
 \end{aligned}$$

In practice this definition is based on a column of water 1 mm height at 4 °C at standard pressure.

*Conventional millimetre of mercury** (mmHg). In accordance with the International Barometric Conventions of the World Meteorological Organization² this is defined as the pressure exerted by a column of liquid 1 mm in height with a density of 13.5951 g cm⁻³ under the standard acceleration due to gravity g_n :

$$\begin{aligned}
 1 \text{ mmHg} &= 0.1 \text{ cm} \times 13.5951 \text{ g cm}^{-3} \times 980.665 \text{ cm s}^{-2} \\
 &= 133.322387 \text{ N m}^{-2} = 1333.22387 \text{ dyn cm}^{-2} \\
 &= 1.0000014 \text{ torr}
 \end{aligned}$$

In practice this definition is based with adequate accuracy on a column of mercury 1 mm in height at 0 °C at standard pressure (1 atm = 101325 N m⁻²).

The noncoherent Anglo-Saxon units of pressure, conventional inch of water (inH₂O), conventional foot of water (ftH₂O) and conventional inch of mercury (inHg), are defined by the formula given for conventional millimetre of water and conventional millimetre of mercury by replacing the metric length unit (0.1 cm) by 1 inch or 1 foot.

For very precise measurements the unit torr is now preferred to the mmHg since unlike the latter the torr is independent of material constants.

Standard pressure in both physics and meteorology is 101325 N m⁻² = 1 atm = 760 torr. It is roughly the mean atmospheric pressure at sea level under the standard acceleration due to gravity.

* The names of these units of pressure actually signify the height h at which the barometer liquid with density ρ under the acceleration due to gravity g exerts the pressure $p = \rho h g$.

Conversion of noncoherent units of pressure

		1 A unit = b B units (b in the table)		
A		B		
Name	Symbol	atm	pdl ft ⁻²	N m ⁻²
millimetre of water.....	mm water	9.67814×10^{-5}	6.58958	9.80638
kilopond per square metre.....	kp m ⁻²	9.67841×10^{-5}	6.58976	9.80665
kilogramme-force per square metre.....	kgf m ⁻²			
pound-force per square foot.....	lbf ft ⁻²	4.72541×10^{-4}	3.21740×10	4.78803×10
torr.....	torr	1.31579×10^{-3}	8.95885×10	1.33322×10^3
conventional inch of water.....	inH ₂ O	2.45832×10^{-3}	1.67380×10^2	2.49089×10^3
conventional foot of water.....	ftH ₂ O	2.94998×10^{-2}	2.00856×10^3	2.98907×10^3
conventional inch of mercury.....	inHg	3.34211×10^{-2}	2.27555×10^3	3.38639×10^3
pound-force per square inch.....	lbf in ⁻²	6.80460×10^{-2}	4.63306×10^3	6.89476×10^3
technical atmosphere.....	at	9.67841×10^{-1}	6.58976×10^4	9.80665×10^4
physical atmosphere.....	atm	1	6.80873×10^4	1.01325×10^5
ton-force per square foot.....	tonf ft ⁻²	1.05849	7.20699×10^4	1.07252×10^5

References

¹ Conférence Générale des Poids et Mesures, *Comptes rendus des séances de la 9^e Conférence générale des Poids et Mesures*, Paris 1948, Gauthier-Villars, Paris, 1949, pages 57 and 89; *Comptes rendus des séances de la 10^e Conférence générale des Poids et Mesures*, Paris 1954, Gauthier-Villars, Paris, 1955, page 79.

² World Meteorological Organization, *International Barometric Conventions*, in British Standards Institution, *Barometer Conventions and Tables*, B.S. 2520: 1954, and in STILLE, U., *Messen und Rechnen in der Physik*, 2nd ed., Vieweg, Braunschweig, 1961.

Energy, Work, Amount of heat

Dimension = L² M T⁻²

Coherent units

International System of Units: joule (J) = newton × metre = m² kg s⁻² = 10⁷ erg = watt second (Ws) (for W see under 'Power', page 214)

CGS system: erg (erg) = dyne × centimetre = cm² g s⁻² = 10⁻⁷ J

ft-lb-s system: foot poundal (ft pdl) = ft² lb s⁻² = 0.0421401101 J

Symbols

Energy = E, W

Potential energy = E_p, V, ϕ

Kinetic energy = E_k, T, K

Work = W, A

Amount of heat = Q

Radiant energy = Q, Q_r, W^r (see also page 222)

Energy, work and amount of heat are physical quantities with the same dimensions and ideally should be measured in a common unit. In the International System of Units this simplification has

conversion of noncoherent units of energy

		1 A unit = B units (B in the table)		
A		B		
Name	Symbol	kWh	ft pdl	J
foot pound-force	ft lbf	3.766×10^{-7}	3.21740×10	1.35582
thermochemical calorie	cal _{th}	1.162×10^{-4}	9.92879×10	4.184
15° calorie	cal ₁₅	1.1626×10^{-4}	9.93234×10	4.1855
International Steam Table calorie	cal _{IT}	1.163×10^{-4}	9.93543×10	4.1868
kilopond metre, kilogramme-force metre	kp m = kgf m	2.72407×10^{-4}	2.32715×10^4	9.80665
liter atmosphere	l atm	2.81451×10^{-4}	2.40448×10^4	1.01325×10^5
British thermal unit	Btu	2.93071×10^{-4}	2.50369×10^4	1.05506×10^5
horsepower-hour	hp h	7.45700×10^{-4}	6.37046×10^4	2.68452×10^6
metric horsepower-hour	ch or PSh	7.3549875×10^{-4}	6.28331×10^4	2.64780×10^6
kilowatt-hour	kWh	1	8.54293×10^7	3.6×10^6

conversion of units of energy used in atomic physics

			1 A unit equals or corresponds to B units (B in the table)		
A			B		
Name	Identifying formula	Symbol	e	J	erg
gramme	$\Delta E(g) = e^2 \times (1g)$	g	1	8.987554×10^{14}	8.987554×10^{14}
joule		J	1.1126×10^{-14}	1	1×10^7
erg		erg	1.1126×10^{-14}	1×10^{-7}	1
atomic mass unit	$\Delta E(u) = e^2 \times (1u)$	u	1.6604×10^{-24}	1.49232×10^{-10}	1.49232×10^{-8}
rydberg	$\Delta E(R_\infty) = e^2 \times (1R_\infty)$	R _y	2.4253×10^{-25}	2.17971×10^{-18}	2.17971×10^{-11}
electronvolt	$\Delta E(eV) = e \times (1V)$	eV	1.7824×10^{-26}	1.60210×10^{-19}	1.60210×10^{-12}
centimetre ⁻¹	$\Delta E(cm^{-1}) = hc \times (1cm^{-1})$	cm ⁻¹	2.2101×10^{-27}	1.98630×10^{-25}	1.98630×10^{-16}
kilvin	$\Delta E(K) = k \times (1K)$	K	1.5361×10^{-27}	1.38054×10^{-23}	1.38054×10^{-16}
second ⁻¹	$\Delta E(s^{-1}) = h \times (s^{-1})$	s ⁻¹	7.3720×10^{-28}	6.62559×10^{-24}	6.62559×10^{-27}
Name	Identifying formula	Symbol	u	ry	eV
gramme	$\Delta E(g) = e^2 \times (1g)$	g	6.0225×10^{23}	4.3233×10^{21}	5.60985×10^{22}
joule		J	6.7010×10^{24}	4.5878×10^{22}	6.24181×10^{24}
erg		erg	6.7010×10^{24}	4.5878×10^{22}	6.24181×10^{24}
atomic mass unit	$\Delta E(u) = e^2 \times (1u)$	u	1	8.4464×10^7	9.31478×10^8
rydberg	$\Delta E(R_\infty) = e^2 \times (1R_\infty)$	R _y	1.4606×10^{-4}	1	1.36054×10
electronvolt	$\Delta E(eV) = e \times (1V)$	eV	1.0736×10^{-6}	7.3500×10^{-8}	1
centimetre ⁻¹	$\Delta E(cm^{-1}) = hc \times (1cm^{-1})$	cm ⁻¹	1.3310×10^{-19}	9.1127×10^{-10}	1.23981×10^{-8}
kilvin	$\Delta E(K) = k \times (1K)$	K	9.2509×10^{-14}	6.3336×10^{-9}	8.61706×10^{-6}
second ⁻¹	$\Delta E(s^{-1}) = h \times (s^{-1})$	s ⁻¹	4.4398×10^{-24}	3.0297×10^{-10}	4.13556×10^{-15}
Name	Identifying formula	Symbol	cm ⁻¹	K	s ⁻¹
gramme	$\Delta E(g) = e^2 \times (1g)$	g	4.5248×10^{23}	6.5102×10^{22}	1.3565×10^{24}
joule		J	5.0345×10^{24}	7.2435×10^{24}	1.5093×10^{24}
erg		erg	5.0345×10^{24}	7.2435×10^{24}	1.5093×10^{24}
atomic mass unit	$\Delta E(u) = e^2 \times (1u)$	u	7.5131×10^{10}	1.0810×10^{10}	2.2524×10^{10}
rydberg	$\Delta E(R_\infty) = e^2 \times (1R_\infty)$	R _y	1.0974×10^8	1.5789×10^8	2.2598×10^{10}
electronvolt	$\Delta E(eV) = e \times (1V)$	eV	8.0657×10^8	1.1605×10^4	2.4180×10^{10}
centimetre ⁻¹	$\Delta E(cm^{-1}) = hc \times (1cm^{-1})$	cm ⁻¹	1	14388	2.9979×10^{10}
kilvin	$\Delta E(K) = k \times (1K)$	K	6.9503×10^{-1}	1	2.0836×10^{10}
second ⁻¹	$\Delta E(s^{-1}) = h \times (s^{-1})$	s ⁻¹	3.3356×10^{-11}	4.7993×10^{-11}	1

now been achieved, and many of the present noncoherent "mechanical", "electrical" and "caloric" units will eventually be of historical interest only. This is likely to take a long time, however, since the

British thermal unit (Btu) is defined as the amount of heat required to raise the temperature of 1 lb of water from 63°F to 64°F. This is a noncoherent unit of energy.

Noncoherent units of energy

The British thermal unit (Btu) is defined as the amount of heat required to raise the temperature of 1 lb of water from 63°F to 64°F. This is a noncoherent unit of energy. The International Steam Table calorie (cal_{IT}) is defined as the amount of heat required to raise the temperature of 1 g of water from 15°C to 16°C. This is a noncoherent unit of energy. The kilowatt-hour (kWh) is defined as the amount of energy consumed by a device with a power of 1 kW operating for 1 hour. This is a noncoherent unit of energy.

= 1000 cal_{IT}

International Steam Table calorie (cal_{IT}) In 1956 the 5th International Conference on Properties of Steam^{2,3,4} redefined the International Steam Table calorie as 1 cal_{IT} = 4.1868 J

Expanded metric horsepower = 735.49875 W

101.3278 J.

British thermal unit (Btu) Like the Steam Table calorie this was redefined in 1956^{2,3,4} as (for lbf see under "Mass", page 204).

$$1 \text{ Btu} = 4.1868 \frac{\text{degF}}{\text{K}} \times \frac{\text{lb}}{\text{g}} = 2.326 \frac{\text{lb}}{\text{g}}$$

Horsepower-hour (hp h) = hp × h, 1 hp = 550 ft lbf s⁻¹ (for lbf see under "Force", page 211)

Metric horsepower-hour (French ch, German PSh) = ch (or PS) × h, 1 ch (or PS) = 75 mkg s⁻¹ (for kg see under "Force", page 211).

Kilowatt-hour (kWh) = kW × h, 1 W = 1 J s⁻¹

Units of energy and energy equivalents in atomic and nuclear physics

The units of energy used in atomic and nuclear physics contain one or more physical constants as factors, namely the velocity of light, c .

energy): gramme [$g \sim E(g)$], atomic mass unit [$u \sim E(u)$], centimetre⁻¹ [$cm^{-1} \sim E(cm^{-1})$], kelvin [$K \sim E(K)$] and second⁻¹ [$s^{-1} \sim E(s^{-1})$]. The relationships of these energy units to those used in macrophysics (joule and erg) depend numerically on the results of determinations of the atomic constants. For the physical constants and other units and measures of energy in atomic and nuclear physics see the table on pages 228 and 229.

References

- 1 Conférence Générale des Poids et Mesures, *Comptes rendus des séances de la 9^e Conférence générale des Poids et Mesures*, Paris 1948, Gauthier-Villars, Paris, 1949, pages 55 and 63.
- 2 STULTZ, U., *Messen und Rechnen in der Physik*, 2nd ed., Vieweg, Braunschweig, 1961.
- 3 International Organization for Standardization, *Quantities and Units of Mechanics*, ISO Recommendation R31, part III, December 1960.
- 4 ROSSINI, F. D., *Nat. Bur. Stand. J. Res.*, 6, 1 (1931); WAGMAN et al., *Nat. Bur. Stand. J. Res.*, 34, 143 (1945).
- 5 Comité International des Poids et Mesures, *Proc. Verb. Com. int. Poids Mes.*, 22, 79 (1950).
- 6 SCHMIDT, E., *Brennstoff, Wärme, Kraft*, 9, 432 (1957).
- 7 COHEN and DU MOND, *Rev. mod. Phys.*, 37, 537 (1965); International Union of Pure and Applied Physics, *Symbols, Units and Nomenclature in Physics*, Document U.I.P. 11 (S.U.N. 65-3), 1965, page 30.

Power (P) (= energy/time = force \times velocity)

Dimension = $L^2 M T^{-3}$

Coherent units

International System of Units: watt (W) = joule per second = newton \times metre per second = $m^2 kg s^{-3} = 10^7$ erg s^{-1} .
CGS system: erg per second (erg s^{-1})
= dyne \times centimetre per second = $cm^2 g s^{-3} = 10^{-7}$ W
ft-lb-s system: foot poundal per second (ft pdl s^{-1}) = $ft^2 lb s^{-3} = 0.0421401101$ W

Conversion of noncoherent units of power

The units of power related to the second (e.g., cal s^{-1}) are converted into ft pdl s^{-1} or watt (= J s^{-1}) by means of the factors given for the conversion of the noncoherent units of energy (page 212).

1 A unit = b B units (b in the table)			
A		B	
Name	Symbol	ft pdl s^{-1}	W = J s^{-1}
International Steam Table calorie per hour	cal _{IT} h ⁻¹	2.75984×10^{-2}	1.163×10^{-3}
British thermal unit per hour	Btu h ⁻¹	6.954 68	2.93071×10^{-1}
horsepower*	hp	1.76957×10^4	7.45700×10^2
metric horsepower*	ch or PS	1.74537×10^4	7.3549875×10^2

* 1 ch or PS = 75 m kp s^{-1} ; 1 hp = 550 ft lbf s^{-1} .

Action (= energy \times time)

Dimension = $L^2 M T^{-1}$

Coherent units

International System of Units: joule \times second (J s)
= newton \times metre \times second = $m^2 kg s^{-1} = 10^7$ erg s
CGS system: erg \times second (erg s)
= dyne \times centimetre \times second = $cm^2 g s^{-1} = 10^{-7}$ J s
ft-lb-s system: foot poundal second (ft pdl s) = $ft^2 lb s^{-1} = 0.0421401101$ J s

Entropy (S)

Dimension = $L^2 M T^{-2} \Theta^{-1}$

Coherent units

International System of Units: joule per kelvin (J K^{-1})
= 10^7 erg K^{-1}

Noncoherent units

erg per kelvin (erg K^{-1}) = 10^{-7} J K^{-1}
foot poundal per degree Fahrenheit (ft pdl degF⁻¹)

Viscosity

Dynamic viscosity (η)

Dimension = $L^{-1} M T^{-1}$

Dynamic viscosity is the property of a fluid (liquid or gas) offering resistance ('internal friction') to the non-accelerated displacement of two adjacent layers.

Coherent units

International System of Units: newton \times second per square metre (N s m^{-2}) = $m^{-1} kg s^{-1} = 0.671969$ pdl s ft^{-2}

CGS system: poise (P) = dyne \times second per square centimetre (dyn s cm^{-2}) = $cm^{-1} g s^{-1} = 10^{-1}$ N s m^{-2}

ft-lb-s system: poundal second per square foot (pdl s ft^{-2})
= $ft^{-1} lb s^{-1} = 1.48816$ N s m^{-2}

Conversion of metric units of dynamic viscosity

		1 A unit = b B units (b in the table)				
A		B				
Name	Symbol	μP	mP	cP	P	N s m^{-2}
micropoise ...	μP	1	10^{-3}	10^{-4}	10^{-6}	10^{-7}
millipoise	mP	10^3	1	10^{-1}	10^{-3}	10^{-4}
centipoise	cP	10^4	10	1	10^{-2}	10^{-3}
poise	P	10^6	10^3	10^2	1	10^{-1}
newton \times second per square metre	N s m^{-2}	10^7	10^4	10^3	10	1

Kinematic viscosity (ν) (= viscosity/density)

Dimension = $L^2 T^{-1}$

MAXWELL's kinematic viscosity is the ratio of the dynamic viscosity η and the density ρ , so that strictly speaking the term viscosity is here a misnomer. ν occurs in many flow processes, particularly when using models, as determinative magnitude (for instance in REYNOLD's number $Re = l u/\nu$).

Coherent units

International System of Units: square metre per second ($m^2 s^{-1}$)
= 10.7639 ft² s^{-1} = 3600 m² h^{-1}

CGS system: stokes (St) = square centimetre per second ($cm^2 s^{-1}$)
= 10^{-4} m² s^{-1}

ft-lb-s system: square foot per second (ft² s^{-1})
= 9.29030×10^{-2} m² s^{-1} = 334.451 m² h^{-1}

Other unit

square metre per hour ($m^2 h^{-1}$) = 2.7×10^{-4} m² s^{-1} = 2.7 St

Viscosity of solutions

The ratio of the viscosity of a solution η to the viscosity of the solvent η_0 is known as the *viscosity ratio* (formerly called relative viscosity) (η/η_0). The quotient $(\eta - \eta_0)/\eta_0$ is the *viscosity increment*. In dilute solutions a further important magnitude is the *viscosity number* (formerly called reduced viscosity) (I_0), dimension $L^3 M^{-1}$, defined as $I_0 = (1/c) \times (\eta - \eta_0)/\eta_0$, where c is the mass concentration of the solution. The limiting value

$$I_0 = \lim_{\substack{c \rightarrow 0 \\ \tau \rightarrow 0}} \frac{1}{c} \times \frac{\eta - \eta_0}{\eta_0}$$

is the *limiting viscosity number* (formerly called intrinsic viscosity) (I_0) (τ = shear stress).

Coherent units for I_0 and I_0

International System of Units: cubic metre per kilogramme ($m^3 kg^{-1}$) = 16.0185 ft³ lb^{-1}

CGS system: cubic centimetre per gramme ($cm^3 g^{-1}$)
= 10^{-3} m³ kg^{-1}

ft-lb-s system: cubic foot per pound (ft³ lb^{-1})
= 0.0624280 m³ kg^{-1}

Surface tension (σ)

Dimension = MT^{-2}

Coherent units

International System of Units: newton per metre (N m^{-1})
= joule per square metre (J m^{-2}) = kg s^{-2}
CGS system: dyne per centimetre (dyn cm^{-1})
= erg per square centimetre (erg cm^{-1}) = g s^{-2} = 10^{-3} N m^{-1}

Thermal conductivity (λ)

Dimension = $\text{LMT}^{-2} \Theta^{-1}$

Coherent unit

International System of Units: watt per (metre \times kelvin)
($\text{W m}^{-1} \text{K}^{-1}$) = $1 \text{ m kg s}^{-3} \text{K}^{-1}$
= $2.38846 \times 10^{-3} \text{ calIT cm}^{-1} \text{s}^{-1} \text{K}^{-1}$
= $0.859845 \text{ kcalIT m}^{-1} \text{h}^{-1} \text{K}^{-1}$
= $1.60497 \times 10^{-4} \text{ Btu ft}^{-1} \text{s}^{-1} \text{degF}^{-1}$

Other unit

erg per (second \times centimetre \times kelvin) ($\text{erg s}^{-1} \text{cm}^{-1} \text{K}^{-1}$)
= $1 \text{ cm g s}^{-3} \text{K}^{-1}$ = $10^{-3} \text{ W m}^{-1} \text{K}^{-1}$
= $2.38846 \times 10^{-3} \text{ calIT cm}^{-1} \text{s}^{-1} \text{K}^{-1}$
= $8.59845 \times 10^{-4} \text{ kcalIT m}^{-1} \text{h}^{-1} \text{K}^{-1}$
= $1.60497 \times 10^{-4} \text{ Btu ft}^{-1} \text{s}^{-1} \text{degF}^{-1}$

Other units with 1 calIT = 4.1868 J

calorie per (centimetre \times second \times kelvin) ($\text{calIT cm}^{-1} \text{s}^{-1} \text{K}^{-1}$)
= $418.68 \text{ W m}^{-1} \text{K}^{-1}$ = $360 \text{ kcalIT m}^{-1} \text{h}^{-1} \text{K}^{-1}$
= $0.0671969 \text{ Btu ft}^{-1} \text{s}^{-1} \text{degF}^{-1}$
kilocalorie per (metre \times hour \times kelvin) ($\text{kcalIT m}^{-1} \text{h}^{-1} \text{K}^{-1}$)
= $1.163 \text{ W m}^{-1} \text{K}^{-1}$ = $2.7 \times 10^{-3} \text{ calIT cm}^{-1} \text{s}^{-1} \text{K}^{-1}$

Anglo-Saxon units with 1 Btu = 232.6 $\frac{\text{lb}}{\text{kg}}$ J = 1055.056 J

British thermal unit per foot second degree Fahrenheit
($\text{Btu ft}^{-1} \text{s}^{-1} \text{degF}^{-1}$) = $6230.64 \text{ W m}^{-1} \text{K}^{-1}$
= $3600 \text{ Btu ft}^{-1} \text{h}^{-1} \text{degF}^{-1}$ = $43200 \text{ Btu in ft}^{-1} \text{h}^{-1} \text{degF}^{-1}$
= $14.8816 \text{ calIT cm}^{-1} \text{s}^{-1} \text{K}^{-1}$

British thermal unit per foot hour degree Fahrenheit
($\text{Btu ft}^{-1} \text{h}^{-1} \text{degF}^{-1}$) = $1.73073 \text{ W m}^{-1} \text{K}^{-1}$
= $2.7 \times 10^{-3} \text{ Btu ft}^{-1} \text{s}^{-1} \text{degF}^{-1}$ = $12 \text{ Btu in ft}^{-1} \text{h}^{-1} \text{degF}^{-1}$
= $1.48816 \text{ kcalIT m}^{-1} \text{h}^{-1} \text{K}^{-1}$

British thermal unit per square foot second degree Fahrenheit

British thermal unit per square foot hour degree Fahrenheit

**(Surface) coefficient of heat transfer (α)
(Over-all) coefficient of heat transfer (K)**

Dimension = $\text{MT}^{-2} \Theta^{-1}$

Coherent unit

SI: watt per (square metre \times kelvin) ($\text{W m}^{-2} \text{K}^{-1}$)
= $1 \text{ kg s}^{-3} \text{K}^{-1}$ = $2.38846 \times 10^{-3} \text{ calIT cm}^{-2} \text{s}^{-1} \text{K}^{-1}$
= $0.859845 \text{ kcalIT m}^{-2} \text{h}^{-1} \text{K}^{-1}$
= $4.89195 \times 10^{-4} \text{ Btu ft}^{-2} \text{s}^{-1} \text{degF}^{-1}$

Other unit

erg per (square centimetre \times second \times kelvin)
($\text{erg cm}^{-2} \text{s}^{-1} \text{K}^{-1}$) = $1 \text{ g s}^{-3} \text{K}^{-1}$ = $10^{-3} \text{ W m}^{-2} \text{K}^{-1}$
= $2.38846 \times 10^{-3} \text{ calIT cm}^{-2} \text{s}^{-1} \text{K}^{-1}$
= $8.59845 \times 10^{-4} \text{ kcalIT m}^{-2} \text{h}^{-1} \text{K}^{-1}$
= $4.89195 \times 10^{-4} \text{ Btu ft}^{-2} \text{s}^{-1} \text{degF}^{-1}$

Other units with 1 calIT = 4.1868 J

calorie per (square centimetre \times second \times kelvin)
($\text{calIT cm}^{-2} \text{s}^{-1} \text{K}^{-1}$) = $4186.8 \text{ W m}^{-2} \text{K}^{-1}$
= $36000 \text{ kcalIT m}^{-2} \text{h}^{-1} \text{K}^{-1}$ = $2.04816 \text{ Btu ft}^{-2} \text{s}^{-1} \text{degF}^{-1}$
kilocalorie per (square metre \times hour \times kelvin)
($\text{kcalIT m}^{-2} \text{h}^{-1} \text{K}^{-1}$) = $1.163 \text{ W m}^{-2} \text{K}^{-1}$
= $2.7 \times 10^{-3} \text{ calIT cm}^{-2} \text{s}^{-1} \text{K}^{-1}$

Anglo-Saxon units with 1 Btu = 232.6 $\frac{\text{lb}}{\text{kg}}$ J = 1055.056 J

Electricity and magnetism (for references see page 217)

International System of Units (SI units)

The base electrical unit is that of electric current, the ampere (A), defined as that constant current which, if maintained in two straight parallel conductors of infinite length, of negligible circular cross-section, and placed one metre apart in vacuum, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

This theoretical definition is realized experimentally in so-called 'absolute ampere measurements' by determining the force between

two parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes. The force F in newtons is given by the equation:

$$F = \frac{\mu_0}{2\pi} \frac{I_1 I_2 l}{r}$$

where μ_0 is the permeability of free space, which is defined as $4\pi \times 10^{-7} \text{ N/A}^2$.

Electrodynamics is now generally described by means of the field theory (as recommended by the IUPAP², IEC³, ISO⁴, etc.) In so

called the 'rationalized' system of units, the unit of electric charge is

defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

The unit of electric charge is the coulomb (C), which is defined as the quantity of electricity which, if maintained in two

parallel conductors of length l metres, separated by a distance r metres, and carrying currents I_1 and I_2 amperes, would produce between these conductors a force equal to 2×10^{-7} newton per metre of length.

Quantity (symbol)	Dimension in LMTI	SI Unit		Numerical value of X in SI unit = $b \times$ numerical value of X_m in emu = $b' \times$ numerical value of X_e in esu			
		Name	Symbol	CGS system			
				electromagnetic (X_m /emu)		electrostatic (X_e /esu)	
				emu	b^*	esu	b'^*
Electric potential difference (U)	$L^2 M T^{-2} I^{-1}$	volt	V	$cm^{3/2} g^{1/2} s^{-2}$	10^{-8}	$cm^{1/2} g^{1/2} s^{-1}$	$\zeta \times 10^{-8}$
Electric current (I)	I	ampere	A	$cm^{1/2} g^{1/2} s^{-1}$	10	$cm^{3/2} g^{1/2} s^{-2}$	$10/\zeta$
Electric current density (j or \mathcal{S})	$L^{-2} I$	ampere per square metre	$A m^{-2}$	$cm^{-3/2} g^{1/2} s^{-1}$	10^5	$cm^{-1/2} g^{1/2} s^{-2}$	$10^5/\zeta$
Electric linear current density (\mathcal{A} or α)	$L^{-1} I$	ampere/metre	$A m^{-1}$	$cm^{-1/2} g^{1/2} s^{-1}$	10^3	$cm^{1/2} g^{1/2} s^{-2}$	$10^3/\zeta$
Electric field strength (E)	$L M T^{-2} I^{-1}$	volt per metre	$V m^{-1}$	$cm^{1/2} g^{1/2} s^{-2}$	10^{-6}	$cm^{-1/2} g^{1/2} s^{-1}$	$\zeta \times 10^{-6}$
Electric flux density, displacement (D)	$L^{-2} T I$	coulomb per square metre	$C m^{-2}$	$cm^{-3/2} g^{1/2}$	$10^5/4\pi$	$cm^{-1/2} g^{1/2} s^{-1}$	$10^5/(4\pi\zeta)$
Electric (displacement) flux (Ψ)	$T I$	coulomb	$C (= A s)$	$cm^{1/2} g^{1/2}$	$10/4\pi$	$cm^{3/2} g^{1/2} s^{-1}$	$10/(4\pi\zeta)$
Electric polarization (P)	$L^{-2} T I$	coulomb per square metre	$C m^{-2}$	$cm^{-3/2} g^{1/2}$	10^5	$cm^{-1/2} g^{1/2} s^{-1}$	$10^5/\zeta$
Electric dipole moment (p)	$L T I$	coulomb \times metre	$C m$	$cm^{3/2} g^{1/2}$	10^{-1}	$cm^{5/2} g^{1/2} s^{-1}$	$10^{-1}/\zeta$
Electric polarizability (α_e)	$M^{-1} T^4 I^2$	farad \times square metre	$F m^2$	$cm s^2$	10^8	cm^3	$10^8/\zeta^2$
Electric susceptibility (χ_e or χ)	$L^0 M^0 T^0 I^0$	1	1	1	4π	1	4π
Electric charge (Q)	$T I$	coulomb	$C (= A s)$	$cm^{1/2} g^{1/2}$	10	$cm^{3/2} g^{1/2} s^{-1}$	$10/\zeta$
Volume density of electric charge, charge density (ρ or η)	$L^{-3} T I$	coulomb per cubic metre	$C m^{-3}$	$cm^{-5/2} g^{1/2}$	10^7	$cm^{-3/2} g^{1/2} s^{-1}$	$10^7/\zeta$
Surface density of electric charge (σ) ..	$L^{-2} T I$	coulomb per square metre	$C m^{-2}$	$cm^{-3/2} g^{1/2}$	10^5	$cm^{-1/2} g^{1/2} s^{-1}$	$10^5/\zeta$
Capacitance (C)	$L^{-2} M^{-1} T^4 I^2$	farad	$F (= A s V^{-1})$	$cm^{-1} s^2$	10^9	cm	$10^9/\zeta^2$
Electric resistance (R)	$L^2 M T^{-2} I^{-2}$	ohm	$\Omega (= V A^{-1})$	$cm s^{-1}$	10^{-9}	$cm^{-1} s$	$\zeta^2 \times 10^{-9}$
(to direct current)							
Electric conductance (G)	$L^{-2} M^{-1} T^2 I^2$	reciprocal ohm**	$A V^{-1}$	$cm^{-1} s$	10^9	$cm s^{-1}$	$10^9/\zeta^2$
(to direct current)							
Electric resistivity (ρ)	$L^2 M T^{-2} I^{-2}$	ohm \times metre	Ωm	$cm^2 s^{-1}$	10^{-11}	s	$\zeta^2 \times 10^{-11}$
Electric conductivity (γ or σ)	$L^{-2} M^{-1} T^2 I^2$	reciprocal ohm** per metre	$A V^{-1} m^{-1}$	$cm^{-2} s$	10^{11}	s^{-1}	$10^{11}/\zeta^2$
Magnetic potential difference (V)	I	ampere	A	$cm^{1/2} g^{1/2} s^{-1}$ (gilbert, Gb)	$10/4\pi$	$cm^{3/2} g^{1/2} s^{-2}$	$10/(4\pi\zeta)$
Magnetic field strength (H)	$L^{-1} I$	ampere per metre	$A m^{-1}$	$cm^{-1/2} g^{1/2} s^{-1}$ (oersted, Oe) [†]	$10^3/4\pi$	$cm^{1/2} g^{1/2} s^{-2}$	$10^3/(4\pi\zeta)$
Magnetic vector potential (A)	$L M T^{-2} I^{-1}$	weber per metre	$Wb m^{-1}$	$cm^{1/2} g^{1/2} s^{-1}$	10^{-6}	$cm^{-1/2} g^{1/2}$	$\zeta \times 10^{-6}$
Magnetic flux density (B)	$M T^{-2} I^{-1}$	tesla	$T (= Wb m^{-2})$	$cm^{-1/2} g^{1/2} s^{-1}$ (gauss, Gs) [†]	10^{-4}	$cm^{-3/2} g^{1/2}$	$\zeta \times 10^{-4}$
(magnetic induction)							
Magnetic flux (Φ)	$L^2 M T^{-2} I^{-1}$	weber	Wb	$cm^{3/2} g^{1/2} s^{-1}$ (maxwell, Mx)	10^{-8}	$cm^{1/2} g^{1/2}$	$\zeta \times 10^{-8}$
Magnetization (M or H_s)	$L^{-1} I$	ampere per metre	$A m^{-1}$	$cm^{-1/2} g^{1/2} s^{-1}$	10^3	$cm^{1/2} g^{1/2} s^{-2}$	$10^3/\zeta$
(Electro)magnetic moment (m or μ) ..	$L^2 I$	ampere \times square metre	$A m^2$	$cm^{3/2} g^{1/2} s^{-1}$	10^{-3}	$cm^{7/2} g^{1/2} s^{-2}$	$10^{-3}/\zeta$
Magnetic susceptibility (χ_m or κ)	$L^0 M^0 T^0 I^0$	1	1	1	4π	1	4π
Magnetic polarization (J or B_i)	$M T^{-2} I^{-1}$	tesla	$T (= Wb m^{-2})$	$cm^{-1/2} g^{1/2} s^{-1}$	$4\pi \times 10^{-4}$	$cm^{-3/2} g^{1/2}$	$4\pi\zeta \times 10^{-4}$
Magnetic dipole moment (p_m)	$L^2 M T^{-2} I^{-1}$	weber \times metre	$Wb m$	$cm^{5/2} g^{1/2} s^{-1}$	$4\pi \times 10^{-10}$	$cm^{3/2} g^{1/2}$	$4\pi\zeta \times 10^{-10}$
(Coulomb's) magnetic pole strength (m) ..	$L^2 M T^{-2} I^{-1}$	weber	$Wb (= V s)$	$cm^{3/2} g^{1/2} s^{-1}$	$4\pi \times 10^{-8}$	$cm^{1/2} g^{1/2}$	$4\pi\zeta \times 10^{-8}$
Self inductance (L)	$L^2 M T^{-2} I^{-2}$	henry	$H (= V s A^{-1})$	em	10^{-9}	$cm^{-1} s^2$	$\zeta^2 \times 10^{-9}$
Permeance (\mathcal{A})	$L^2 M T^{-2} I^{-2}$	henry	$H (= V s A^{-1})$	em	$4\pi \times 10^{-9}$	$cm^{-1} s^2$	$4\pi\zeta^2 \times 10^{-9}$
De-electrification or demagnetization factor (N)	$L^0 M^0 T^0 I^0$	1	1	1	$1/4\pi$	1	$1/4\pi$
Electric or magnetic force (F) ^{††}	$L M T^{-2}$	newton	$N (= J m^{-1})$	$cm g s^{-2} = \text{dyn}$	10^{-5}	$cm g s^{-2} = \text{dyn}$	10^{-5}
Electric or magnetic energy (W) ^{††}	$L^2 M T^{-2}$	joule	$J (= V A s)$	$cm^2 g s^{-2} = \text{erg}$	10^{-7}	$cm^2 g s^{-2} = \text{erg}$	10^{-7}
Electric or magnetic energy density... (w) ^{††}	$L^{-1} M T^{-2}$	joule per cubic metre	$J m^{-3}$	$cm^{-1} g s^{-2}$	10^{-1}	$cm^{-1} g s^{-2}$	10^{-1}
Electric or magnetic power (P) ^{††}	$L^2 M T^{-3}$	watt	$W (= V A)$	$cm^2 g s^{-3}$	10^{-7}	$cm^2 g s^{-3}$	10^{-7}
Poynting vector (S) (surface density of power in an electromagnetic wave)	$M T^{-3}$	watt per square metre	$W m^{-2}$	$g s^{-3}$	10^{-3}	$g s^{-3}$	10^{-3}

* $\zeta = 2.997\,925 \times 10^{10}$ ($3\sigma = \pm 3 \times 10^2 \text{ ms}^{-1}$)
 $1/\zeta = 3.335\,640 \times 10^{-11}$
 $\zeta^2 = 8.987\,55 \times 10^{20}$
 $1/\zeta^2 = 1.112\,650 \times 10^{-21}$
 $4\pi = 1.256\,637 \times 10$

$1/4\pi = 7.957\,75 \times 10^{-2}$
 $4\pi\zeta = 3.767\,304 \times 10^{11}$
 $1/4\pi\zeta = 2.654\,418 \times 10^{-12}$
 $4\pi\zeta^2 = 1.129\,409 \times 10^{22}$
 $1/4\pi\zeta^2 = 8.854\,19 \times 10^{-23}$

** Often called 'mho'. The name siemens, adopted by the IEC in 1935, will come up for approval as name of the SI unit of conductance at the next General Conference of Weights and Measures.

[†] The names oersted and gauss are often interchanged.

^{††} See also under 'Force', 'Energy' and 'Power', pages 211–214.

References see page 221)

The unit of activity in the International System of Units (of the reciprocal second (s^{-1})); the commonly used unit is the curie (Ci):

$$1 \text{ Ci} = 3.7 \times 10^{10} \text{ s}^{-1}$$

Decimal multiples and submultiples of the curie are

$$1 \text{ megacurie (MCi)} = 10^6 \text{ Ci} = 3.7 \times 10^{16} \text{ s}^{-1}$$

$$1 \text{ kilocurie (kCi)} = 10^3 \text{ Ci} = 3.7 \times 10^{13} \text{ s}^{-1}$$

$$1 \text{ millicurie (mCi)} = 10^{-3} \text{ Ci} = 3.7 \times 10^{10} \text{ s}^{-1}$$

$$1 \text{ microcurie (μCi)} = 10^{-6} \text{ Ci} = 3.7 \times 10^4 \text{ s}^{-1}$$

$$1 \text{ nanocurie (nC)} = 10^{-9} \text{ Ci} = 3.7 \times 10^1 \text{ s}^{-1}$$

$$1 \text{ picocurie (pCi)} = 10^{-12} \text{ Ci} = 3.7 \times 10^{-2} \text{ s}^{-1}$$

4. Specific activity

The specific activity a of a radioactive material (for instance a radioactive solution) is the activity A of the radionuclide contained divided by the mass m of the material,

$$a = \frac{A}{m}$$

This quantity is a characteristic constant of the radionuclide expressing the maximum specific activity attainable (i.e., in the carrier free state)*

$$a = \frac{\lambda N_A}{M}$$

$$= 1.63 \times 10^{15} \frac{\lambda}{A_r} \text{ Ci g}^{-1}$$

where N_A is the Avogadro constant, M the molar mass in grams per mole (see page 227) of the radionuclide, A_r its relative atomic mass (see page 226) and λ the value of its decay constant in s^{-1}

Table 1 Reciprocals of the specific activities of some radionuclides

Nuclide	$T_{1/2}$	$1/a$ in g Ci^{-1}
^{24}Na	14.8 h	0.000 000 11 ³
^{131}I	8.06 d	0.000 008 1
^{32}P	14 d	0.000 003 52
^{45}Ca	164 d	0.000 056 6
^{14}C	5570 a	0.187

The activity concentration of a radioactive material (liquid or gas, at a given temperature and pressure) is the ratio of the activity of the contained radionuclide to the volume of the material. The commonly used unit is the curie per litre (Ci l^{-1}) or a decimal multiple of it. A special unit of activity concentration used in biology for the activity concentration of water containing ^{222}Rn is the eman.

$$1 \text{ eman} = 10^{-18} \text{ Ci l}^{-1}$$

The MACH unit formerly in common use is equal to 3.6 eman

Radiation dosimetry

A long discussion on radiological quantities and units ended in 1962 with the general acceptance of the definitions recommended by the International Commission on Radiological Units and Measurements (ICRU).

For comprehensive surveys of the physical concepts and quantities in the dosimetry of ionizing radiations as well as the quantities characterizing radiation sources and radiation fields see the literature^{2, 3}.

* In English-speaking countries other units are used.

Radioactivity

1. Basic concepts

The term *nuclide* indicates a species of atom having specified numbers of protons and neutrons in its nucleus. Nuclides of one and the same chemical element, i.e., nuclides with the same number of protons and differing only in the number of neutrons, are known as *isotopes* of the element concerned. In some nuclides various energy states of the nucleus with finite lifetimes are possible. These states are called *isomers* of the nuclide. Isomeric nuclides have the same numbers of protons and neutrons and differ only in their energy content and thus their lifetime.

The nature of a nuclide is indicated unambiguously by the chemical symbol of the element and the number of nucleons (sum of the protons and neutrons = mass number) shown as an upper index to the left of the element symbol (e.g., ^{12}C , ^{32}P). Additionally, the number of protons (atomic number) can be given as a lower index on the left. Isomers in an excited, metastable state are indicated by a right upper index 'm' (e.g., $^{99\text{m}}\text{Tc}$).

2. Radioactivity and law of disintegration

Radioactivity is the property of certain nuclides of spontaneously emitting either particles or gamma rays from the nucleus (nuclear radiation) or X rays from the shell after capture of an electron from the shell by the nucleus (characteristic X radiation). Except for isomeric transitions, this process always results in a change in the nature of the nuclide (radioactive transformation or radioactive disintegration). Nuclides possessing this property are known as radionuclides.

It is impossible to predict the time when an individual atom will

$$-dN = \lambda N dt$$

If at time zero N_0 atoms of an isolated radionuclide are present the number N_t of atoms not yet disintegrated at any time t is given by

$$N_t = N_0 e^{-\lambda t}$$

In equal time intervals the number of radioactive atoms decreases by the same proportion, the time interval during which the number decreases by half is known as the *half-life* ($T_{1/2}$)

$$T_{1/2} = \frac{\ln 2}{\lambda} = \frac{0.693}{\lambda}$$

The reciprocal of the decay constant λ has the dimension of time and is known as the *mean lifetime*. τ is the time during which the number of atoms of a radionuclide falls to the fraction $1/e$ ($\approx 37\%$) of its original value.

3. Activity

The quantity $-(dN/dt) = \lambda N_t$, i.e., the number of radioactive transformations taking place in a sample during the time dt divided by this time interval, is called the *activity* A . It is a measure of the

1. Introductory

In accordance with the fundamental GROTTIUS-DRAPER law for radiation of any kind, when matter is traversed by energy-rich radiation only that part of the energy that is absorbed can have an action on the matter. With ionizing radiations this absorption of energy occurs in several stages⁶ before it becomes evident biologically. It has been agreed internationally that 'energy imparted to matter' shall be understood to mean only that energy manifested as excitation, ionization or change in the chemical bond energy of the atoms or molecules. This dosimetrically important quantity is defined² as follows:

The energy E_D imparted by ionizing radiation to the matter in a volume is the difference between the sum E_{in} of the energies (exclusive of rest energies) of all the directly and indirectly ionizing particles which have entered the volume and the sum E_{ex} of the energies (exclusive of rest energies) of all those which have left it, minus the energy equivalent Q of any increase in rest mass that took place in nuclear or elementary particle reactions within the volume:

$$E_D = \sum E_{in} - \sum E_{ex} + \sum Q$$

Whereas there can be no confusion concerning the energy totals E_{in} and E_{ex} it is necessary in the case of Q to be quite clear as to whether the nuclear or elementary particle reaction is exothermic or endothermic, i.e., whether Q is positive or negative. For example, the absorption of a photon in the volume concerned may produce an electron pair (electron + positron), an endothermic process; for this reaction therefore $Q = +2m_e c^2$ (m_e is the rest mass of the electron, c the velocity of light) for each interaction.

The absorbed dose is the amount of energy E_D imparted to the matter divided by the mass m of the matter (see below). The most important task of dosimetry is to determine this absorbed dose, which is now regarded as the most meaningful quantity to which the observable chemical and biological effects can be related. The absorbed dose is the result of certain physical reactions between radiation and matter, reactions that are in turn dependent on the nature, intensity and spectral energy distribution of the radiation and the atomic composition of the material.

Radiation fields in the body are usually non-uniform in space as well as in time. Thus there may be non-uniform distribution of the absorbed dose at the boundary surfaces of soft tissues or bones, while the pulsed electrons from particle accelerators constitute radiation non-uniform in time. The quantities concerned must therefore be determined for regions of space or intervals of time so small that any further reduction would not appreciably change the values of the quotients measured. This requirement necessitates the use of some limiting procedure, and in the ICRU definitions² the quantities are presented as quotients of small differences. As the ICRU Reports² point out, the region of space considered also has a lower limit of size, for it must still be large enough to contain many interactions and be traversed by many particles. If it is impossible to find a mass fulfilling both these conditions the dose has to be deduced from multiple measurements involving extrapolation or averaging procedures. The symbol Δ is placed before symbols for quantities concerned in such averaging procedures.

2. Radiation field quantities

A radiation field is a region in vacuum or matter that is traversed by radiation.

$$2.1 \text{ Particle fluence } \Phi = \frac{\Delta N}{\Delta a}$$

where ΔN is the number of particles* entering a sphere of cross-sectional area Δa .

$$2.2 \text{ Particle flux density or particle fluence rate } \varphi = \frac{\Delta \Phi}{\Delta t}$$

where $\Delta \Phi$ is the particle fluence in time Δt .

$$2.3 \text{ Energy fluence } \Psi = \frac{\Delta E_\psi}{\Delta a}$$

where ΔE_ψ is the sum of the energies, exclusive of rest energies, of all the particles entering a sphere of cross-sectional area Δa .

$$2.4 \text{ Energy flux density or energy fluence rate } \psi = \frac{\Delta \Psi}{\Delta t}$$

where $\Delta \Psi$ is the energy fluence in the time Δt .

3. Interactions

Since the great majority of radiations used in medicine are X ray gamma rays or electrons discussion will be limited here to the interactions of photons and electrons with matter. Neutron/matter interactions and neutron dosimetry fall outside the scope of the present article.

3.1 When photons collide with atoms or molecules, electrons are liberated (as a result of the photoelectric effect, COMPTON effect and pair production) and absorb some of the energy of the photons.

$$\text{Mass energy transfer coefficient } \frac{\mu_K}{\rho} = \frac{1}{E} \cdot \frac{\Delta E_K}{\Delta l}$$

where ΔE_K is the sum of the kinetic energies of the secondary electrons liberated in a layer of thickness Δl and density ρ , and E is the sum of the energies (excluding rest energies) of the photons incident normally upon the layer.

3.2 When charged particles collide with atoms or molecules, part of their kinetic energy is lost in collisions with atoms or molecules due to ionization, electronic excitation and production of bremsstrahlung.

$$\text{Mass stopping power } \frac{S}{\rho} = \frac{1}{E} \cdot \frac{\Delta E}{\Delta l}$$

where ΔE is the average amount of energy lost by a charged particle of energy E when traversing a path of length Δl in a layer of density ρ .

$$S_e/\rho = \text{electron mass stopping power}$$

4. Quantities and units of dose

4.1 Absorbed dose and absorbed dose rate

4.1.1 The absorbed dose* D produced by ionizing radiation in matter is the quotient of ΔE_D by Δm , where ΔE_D is the energy imparted by the radiation to the matter in a volume element and $\Delta m = \rho \times \Delta V$ is the mass of the matter in that volume element:

$$D = \frac{\Delta E_D}{\Delta m} = \frac{1}{\rho} \cdot \frac{\Delta E_D}{\Delta V}$$

The expression 'integral absorbed dose' still in common use thus simply means the amount of energy imparted to matter (see under 1. above):

$$E_D = \sum_i (D_i \cdot \Delta m_i)$$

In medical radiology 'matter' could for instance be a single organ or the whole body. The term 'energy imparted to matter' is much to be preferred from the point of view of clarity.

The special unit of absorbed dose is the rad (rd):

$$1 \text{ rd} = 0.01 \text{ J kg}^{-1} = 100 \text{ erg g}^{-1} = 2.388 \times 10^{-6} \text{ calit g}^{-1} = 6.242 \times 10^{13} \text{ eV g}^{-1}$$

4.1.2 The absorbed dose rate \dot{D} is the quotient of ΔD by Δt , where ΔD is the increment in absorbed dose in the time Δt :

$$\dot{D} = \frac{\Delta D}{\Delta t}$$

When the conditions are such that there is no variability in time $\dot{D} = D/t$.

Special units of absorbed dose rate are rad per second (rd s⁻¹), rad per minute (rd min⁻¹), rad per hour (rd h⁻¹), etc.:

$$1 \text{ rd s}^{-1} = 0.01 \text{ W kg}^{-1}$$

The direct measurement of absorbed dose or absorbed dose rate is possible only by means of calorimetry in phantoms and is very time-consuming. In practical dosimetry indirect methods are used, particularly those based on ionization measurements in air, in which the absorbed dose is obtained by simple calculation.

* In this chapter the expression 'particle' is understood to include not only corpuscles like electrons, protons, neutrons, etc. but also photons.

* The designation 'absorbed dose' has been criticized on the grounds that an 'absorbed dose' can be produced only in matter and not in vacuum. For this reason this quantity is known in the German literature as 'energy dose'.

2 Exposure and exposure rate

4.2.1 The *exposure* (X) is the quotient of ΔQ by Δm , where ΔQ

$$X = \frac{\Delta Q}{\Delta m}$$

The special unit of exposure is the roentgen** (R), defined as

$$1 \text{ R} = 2.58 \times 10^{-4} \text{ C kg}^{-1} \text{ (exactly)}$$

From the definition of the roentgen and the elementary charge $e = 1.602 \times 10^{-19} \text{ C}$ it follows that an exposure of 1 R produces

same methods as exposure and has the same numerical value when expressed in roentgen.

Secondary electron equilibrium exists at a point in matter when the sum of the kinetic energies of the photon-produced secondary electrons entering a volume containing this point is equal to the sum of the kinetic energies of the secondary electrons leaving this volume. This equilibrium can be established in an ionization chamber by enclosing the volume of air by a wall equivalent to air, for instance graphite, of a thickness at least equal to the range of the secondary electrons in this wall. A further condition is that the mean range of the photon-produced secondary electrons is small compared to $1/\mu$ (μ being the linear attenuation coefficient for the photons). Since this second condition is approximately fulfilled only for photons of energies up to about 3 MeV the equilibrium ion dose can be measured only when the photon energy is below this level. The introduction of the ionization chamber must not noticeably disturb the radiation field of the photons.

4.2.2 The *exposure rate* (\dot{X}) is the quotient of ΔX by Δt , where ΔX is the increment in exposure in time Δt .

$$\dot{X} = \frac{\Delta X}{\Delta t}$$

When the conditions are such that there is no variability in time $X = \dot{X}t$.

Special units of exposure rate are roentgen per second (R s⁻¹), roentgen per minute (R min⁻¹), roentgen per hour (R h⁻¹), etc.

$$1 \text{ R s}^{-1} = 2.58 \times 10^{-4} \text{ A kg}^{-1}$$

Not included in the ICRU Reports³ but appearing in the appropriate German DIN Standard⁴ is the quantity 'ion dose', applicable to all kinds of radiation except neutrons.

4.2.3 The *ion dose* I produced by ionizing radiation in matter is the quotient of ΔQ by Δm_A , where ΔQ is the electric charge of the ions of one sign formed directly or indirectly by the radiation in air in a volume element ΔV , and Δm_A is the mass of the air of density ρ_A in that volume element

$$I = \frac{\Delta Q}{\Delta m_A} = \frac{1}{\rho_A} \frac{\Delta Q}{\Delta V}$$

The special unit of ion dose is likewise the roentgen (see above). From the definition of the roentgen and the elementary charge $e = 1.602 \times 10^{-19} \text{ C}$ it follows that an ion dose of 1 R produces 1.610×10^{13} ion pairs per gramme (2.082×10^8 ion pairs per cubic centimetre) of air at its normal density of 1.293 mg cm^{-3} .

4.2.4 The *ion dose rate* \dot{I} is the quotient of ΔI by Δt , where ΔI is the increment in ion dose in time Δt .

$$\dot{I} = \frac{\Delta I}{\Delta t}$$

When the conditions are such that there is no variability in time $I = \dot{I}t$.

The special units of ion dose rate are roentgen per second (R s⁻¹), roentgen per minute (R min⁻¹), roentgen per hour (R h⁻¹), etc.

Table 2 Conversion of common units of exposure rate and ion dose rate

	mR h ⁻¹	μR s ⁻¹	R h ⁻¹	R min ⁻¹	R s ⁻¹
1 mR h ⁻¹	1	2.8×10^{-1}	10^{-3}	1.7×10^{-3}	2.8×10^{-7}
1 μR s ⁻¹	3.6	1	3.6×10^{-1}	6×10^{-3}	10^{-6}
1 R h ⁻¹	10^3	2.8×10^3	1	1.7×10^{-1}	2.8×10^{-4}
1 R min ⁻¹	6×10^3	1.7×10^4	60	1	1.7×10^{-2}
1 R s ⁻¹	3.6×10^4	10^4	3.6×10^3	60	1

instance (11) the Bragg-Gray conditions are fulfilled when

- the flux density of the first generation of electrons and their energy distribution remain unchanged by the cavity filled with material B,
- the energy of the secondary electrons produced by the photons in material B is negligible in comparison with the energy imparted to material B,
- the flux density of the electrons of all generations within the material B is uniform throughout.

These conditions can be approximately met if the cavity contains air and its linear dimensions are small compared with $1/\mu$ (μ being the linear attenuation coefficient for the photons) and compared with the mean range of the secondary electrons. The walls of such a cavity ionization chamber must either be very thin or have values for mass energy transfer coefficient μ_{en}/ρ and electron mass stopping power S_{en}/ρ deviating only slightly from those of the surrounding material A. In other words, the ionization of the air molecules in the cavity by the photons must be due predominantly to the secondary electrons produced in the surrounding material A. In order to reduce boundary layer effects between the material of the wall and the air in the cavity resulting from low-energy delta-electrons the inner side of the wall must be covered with a graphite layer about 1 μm thick. If this is not done the mean cavity ion dose will be dependent on the volume in which the dose is being measured.

5. Conversion of dose quantities

5.1 The absorbed dose D_A for air is obtained from the ion dose I (measured as I_s or I_e)

$$D_A = U_{AB} \cdot I$$

where $U_{AB} = 0.869 \text{ rd/R}$ is the ionization constant of air, obtained from the average energy E_1 ($= 33.7 \text{ eV}$) required for the formation of an ion pair in air, from the elementary charge e and from the relationship $1 \text{ V} = 1 \text{ J/C} = 2.58 \times 10^{-4} \text{ rd R}^{-1}$. Above about 10 keV, U_{AB} remains practically constant over a wide energy range.

5.2 For photon irradiation the absorbed dose D_A at the point of interest in material Z is obtained from the absorbed dose D_A at the same point with secondary electron equilibrium in air (see paragraph 4.2.1.1 above) in accordance with the relationship

$$D_A = D_A \cdot (\mu_{en}/\rho)_Z / (\mu_{en}/\rho)_A$$

where $(\mu_{en}/\rho)_Z$ and $(\mu_{en}/\rho)_A$ are the mass energy transfer coefficients (see paragraph 3.1, page 218) of the material Z (for instance body tissues) and air respectively for photons of energy E . For a photon spectrum the values $(\mu_{en}/\rho)_Z$ and $(\mu_{en}/\rho)_A$ averaged over the spectrum must be used instead.

For the exposure X^{**} the conversion equations are as follows

(a) for photons of uniform energy E :

$$D_A = f \cdot X, \text{ with } f = U_{AB} \cdot (\mu_{en}/\rho)_Z / (\mu_{en}/\rho)_A$$

(b) for a photon spectrum.

$$D_A = \bar{f} \cdot X, \text{ with } \bar{f} = U_{AB} \cdot (\bar{\mu}_{en}/\rho)_Z / (\bar{\mu}_{en}/\rho)_A$$

Values of the conversion factor f and \bar{f}

* Or exposure X (see paragraph 4.2.1.1).

** Or equilibrium ion dose I_s (see paragraph 4.2.1.1), in which case I_s must replace X in the formulae.

** This unit is numerically identical with the old roentgen (R), defined as 1 electrostatic unit of charge per 1.293 mg of air.

sorbed dose D_A for air measured at the same point under Bragg-Gray conditions (see paragraph 4.2.5 above) in accordance with the relationship

$$D_Z = D_A \cdot (\bar{S}_e/e)_Z / (\bar{S}_e/e)_A$$

where $(\bar{S}_e/e)_Z$ and $(\bar{S}_e/e)_A$ are the electron mass stopping powers (see paragraph 3.2, page 218) of the material Z and of air averaged over the electron spectrum. Using the cavity ion dose J_e the conversion equation is as follows:

$$D_Z = \bar{g} \cdot J_e, \text{ with } \bar{g} = U_{1A} \cdot (\bar{S}_e/e)_Z / (\bar{S}_e/e)_A$$

Values of the conversion factor \bar{g} for air, water and soft tissues are given in Table 5.

6. Relation of absorbed dose to radiation field

6.1 For photons of uniform energy the energy flux density φ_{ph} of the photons at the point of interest is related to the absorbed dose

rate \dot{D} at the same point when there is secondary electron equilibrium as follows:

$$\dot{D} = (\mu_K/e) \cdot \varphi_{ph}$$

Similarly, for the absorbed dose D and the energy fluence Ψ_{ph} of the photons,

$$D = (\mu_K/e) \cdot \Psi_{ph}$$

where μ_K/e is the mass energy transfer coefficient of the material for photons of this energy.

6.2 For electrons of uniform energy the particle flux density φ_e of the electrons at the point of interest is related to the absorbed dose rate \dot{D} at the same point under BRAGG-GRAY conditions as follows:

$$\dot{D} = (S_e/e) \cdot \varphi_e$$

Table 3 Conversion factor $f = D/X$

E in MeV	f in rd R ⁻¹ for			
	Air	Water*	Soft tissues**	Bone (compact)**
0.010	0.869	0.912	0.925	3.54
0.015	0.869	0.890	0.916	3.97
0.020	0.869	0.877	0.916	4.23
0.030	0.869	0.870	0.910	4.39
0.04	0.869	0.873	0.919	4.14
0.05	0.869	0.893	0.926	3.58
0.06	0.869	0.915	0.929	2.91
0.08	0.869	0.937	0.939	1.91
0.10	0.869	0.942	0.948	1.45
0.15	0.869	0.964	0.956	1.05
0.20	0.869	0.971	0.963	0.979
0.30	0.869	0.964	0.957	0.938
0.4	0.869	0.967	0.954	0.928
0.5	0.869	0.964	0.957	0.925
0.6	0.869	0.964	0.957	0.925
0.8	0.869	0.967	0.956	0.920
1.0	0.869	0.967	0.956	0.922
1.5	0.869	0.966	0.958	0.920
2.0	0.869	0.966	0.954	0.921
3.0	0.869	0.964	0.954	0.928

* From National Bureau of Standards, Report 8681, U.S. Government Printing Office, Washington, 1965.

** From National Bureau of Standards, *Physical Aspects of Irradiation*, ICRU Report 10b, 1962, Handbook 85, U.S. Government Printing Office, Washington, 1964.

Table 5 Conversion factor $\bar{g} = D/J_e$

Radiation		\bar{g} in rd R ⁻¹ for		
Quantum energy or electron energy	Half-value layer or radionuclide	Air	Water	Soft tissues
(a) Bremsstrahlung at 400 kV tube potential				
0.66 MeV	4.2 mm Cu	0.87	1.01	1.00
1.25 MeV	¹³⁷ Cs	0.87	1.00	1.00
Bremsstrahlung 15 MeV	⁶⁰ Co	0.87	0.99	0.99
Bremsstrahlung 30 MeV	-	0.87	0.98	0.97
Bremsstrahlung 45 MeV	-	0.87	0.95	0.94
(b) Electrons				
5 MeV	-	0.87	0.92	0.91
10 MeV	-	0.87	0.88	0.87
20 MeV	-	0.87	0.84	0.83
30 MeV	-	0.87	0.82	0.81
40 MeV	-	0.87	0.81	0.80
50 MeV	-	0.87	0.80	0.79

When calculating the absorbed dose for soft tissues embedded in bone the factor for the latter should be used since the effect of bone has already been allowed for in measurement of the cavity ion dose.

Values (a) from National Bureau of Standards, *Physical Aspects of Irradiation*, ICRU Report 10b, 1962, Handbook 85, U.S. Government Printing Office, Washington, 1964; (b) calculated from BERGER and SELTZER, *Tables of Energy Losses and Ranges of Electrons and Positrons*, NASA SP-3012, National Aeronautics and Space Administration, Washington, 1964, and *Additional Stopping Power and Range Tables for Protons, Muons and Electrons*, NASA SP-3036, National Aeronautics and Space Administration, Washington, 1966.

Table 4 Conversion factor $\bar{f} = D/X$

Tube potential in kV	Radiation				\bar{f} in rd R ⁻¹ for			
	Filter		Half-value layer		Air	Water	Soft tissues	Bone (compact)
	mm Al	mm Cu	mm Al	mm Cu				
50	1.4	-	1.2	0.03	0.87	0.88	0.93	4.2
100	-	0.2	4.2	0.18	0.87	0.89	0.92	3.6
150	-	0.5	-	0.75	0.87	0.92	0.94	2.3
200	-	1.0	-	1.45	0.87	0.94	0.95	1.6
250	-	1.5	-	2.35	0.87	0.95	0.95	1.4
300	-	3.0	-	3.5	0.87	0.96	0.95	1.2
400	-	3.0	-	4.2	0.87	0.96	0.96	1.1

When calculating the absorbed dose for soft tissues embedded in bone from the measured exposure a value of \bar{f} should be chosen lying between those for soft tissues and bone and depending on the distance of the bone from

the point of measurement (cf. National Bureau of Standards, *Physical Aspects of Irradiation*, ICRU Report 10b, 1962, Handbook 85, U.S. Government Printing Office, Washington, 1964).

ularly, for the absorbed dose D and the particle fluence Φ_e of electrons,

$$D = (S_e/\rho) \cdot \Phi_e$$

where S_e/ρ is the electron mass stopping power of the material for electrons of this energy.

Since the coefficients μ_{en}/ρ and S_e/ρ are themselves functions of

an energy spectrum, in which case mean values of the coefficients over the spectral range must be used.

Relative biological effectiveness (RBE)

At present hard filtered 200 kV X rays produce the same effect under otherwise identical conditions. The RBE factor is not a constant for a particular kind of radiation since different values are obtained depending on the nature of the radiation reaction being observed, on the kind of biological system under study, on the stage of development of the object being radiated, and on the distribution of the absorbed dose in space and time.⁷ Since the RBE factor is such is unsuitable for use in the field of radiation protection the ICRU⁸ has recommended that the term RBE should be employed in radiobiology only.

$$\xi = D_0/D$$

where D is the absorbed dose of the radiation under consideration which produces a particular biological effect, and D_0 the absorbed dose of a standard radiation (at present hard filtered 200 kV X rays) which produces the same effect under otherwise identical conditions. The RBE factor is not a constant for a particular kind of radiation since different values are obtained depending on the nature of the radiation reaction being observed, on the kind of biological system under study, on the stage of development of the object being radiated, and on the distribution of the absorbed dose in space and time.⁷ Since the RBE factor is such is unsuitable for use in the field of radiation protection the ICRU⁸ has recommended that the term RBE should be employed in radiobiology only.

Dose equivalent and quality factor⁹

In radiation protection the place of the RBE factor ξ is taken by the quality factor⁹ q , and that of the absorbed dose of the standard radiation⁹ which is not used in radiation protection – by the dose equivalent⁹ D_e , defined as follows:

$$D_e = q \cdot D$$

The concept of dose equivalent is intended for use in radiation protection only. The quality factor q is a dimensionless number whose magnitude depends mainly on the nature of the radiation, the particle energy and the conditions under which the irradiation takes place. In practice, agreed conventional values of q are used based on the relative biological effectiveness ξ . The dose equivalent is equal to the absorbed dose produced by a standard radiation with a quality factor $q = 1$ (at present 200 kV X rays), this absorbed dose is considered from the point of view of risk to be the same as the absorbed dose produced by the actual radiation with a quality factor $q \neq 1$.

⁹ The symbol QF used in the ICRU Reports⁸, like the symbol DE for dose equivalent, is inconvenient for use in formulae.

Table 6 Specific gamma ray constants of some radionuclides

$\Gamma_{\text{m}} \text{ R h}^{-1} \text{ m}^2 \text{ Ci}^{-1}$											
²² Na	²⁴ Na	⁴⁰ K	⁵¹ Cr	⁵⁵ Co	⁵⁷ Co	⁶⁰ Co	⁶⁴ Cu	¹³⁷ I	¹³⁷ I	¹³⁷ Cs + ¹³⁷ Ba ^m	¹³⁷ La
1.19	1.84	0.14	0.63	0.55	1.31	0.12	1.22	0.22	0.31	0.50	0.23

References

- Conférence Générale des Poids et Mesures, *Comptes rendus des séances de la 12^e Conférence générale des Poids et Mesures*, Paris 1964, Gauthier-Villars, Paris, 1964, page 94.
- Quarman et al., *Radiation Interactions in Chemical Processes*, Lea & Febiger, Philadelphia, 1958.

If a number of different radiations are present simultaneously the total dose equivalent is the sum of the dose equivalents of the individual radiations:

$$D_e = \sum_i D_{ei} = \sum_i (D_i q_i)$$

For dose equivalents the unit rad is given the special name rem (symbol rem):

$$1 \text{ rem} = 1 \text{ rd}$$

The term rem is reserved exclusively for expressing dose equivalents, so that data given in this unit are immediately recognizable as such.

9. Specific gamma ray constant

The specific gamma ray constant Γ of a gamma-emitting radionuclide is the quotient of $\dot{H} \times \Delta X$ by the activity A of the nuclide, where ΔX is the exposure rate at a distance l from a point source of the nuclide and the gamma rays are assumed to undergo no absorption either in the sample or over the distance l .

$$\Gamma = \frac{\dot{H} \cdot l^2}{A}$$

\dot{H} is normally only the exposure rate resulting from gamma radiation and from the annihilation radiation of positron-emitting nuclides. If the X rays due to internal conversion or electron capture are not included this must be clearly stated when giving the specific

$$\Gamma_{\text{m}} = \frac{\dot{H} \cdot l^2}{m}, \text{ numerically } \Gamma_{\text{m}} = 0.825 \text{ R h}^{-1} \text{ m}^2 \text{ g}^{-1}$$

The special unit of specific gamma ray constant is

$$\frac{\text{roentgen} \times \text{square metre}}{\text{hour} \times \text{curie}} \quad (\text{R h}^{-1} \text{ m}^2 \text{ Ci}^{-1})$$

For ²²⁶Ra the unit is

$$\frac{\text{roentgen} \times \text{square metre}}{\text{hour} \times \text{gramme}} \quad (\text{R h}^{-1} \text{ m}^2 \text{ g}^{-1})$$

If the activity A or the mass m_{Ra} of the radium is known the exposure rate at the distance l can therefore be calculated providing absorption of the gamma rays in the source and intervening air is neglected

$$\dot{H} = \Gamma \frac{A}{l^2} \quad \text{or} \quad \dot{H} = \Gamma_{\text{m}} \frac{m_{\text{Ra}}}{l^2}$$

ington, 1964

Quantity* and definition†	SI Unit	
	Name	Symbol
Electromagnetic radiation (radiant quantities)		
The radiant energy Q_e (or W) is the energy emitted, transferred or received as radiation.	joule	J
The radiant energy density w is the radiant energy in an element of volume divided by that element: $w = dQ_e/dV$.	joule per cubic metre	J m ⁻³
The radiant flux or radiant power Φ_e is the power emitted, transferred or received as radiation: $\Phi_e = P = dQ_e/dt$.	watt	W
The spectral concentration of radiant flux** $\Phi_{e,\lambda}$ is a spectral distribution function of radiant flux, i.e., the radiant flux in an infinitesimal wave-length interval divided by the range of that interval: $\Phi_e = \int \Phi_{e,\lambda} d\lambda$. $\Phi_{e,\lambda}$ is often given in watt per nanometre ($1 \text{ W nm}^{-1} = 10^9 \text{ W m}^{-1}$).	watt per metre	W m ⁻¹
The radiant intensity I_e of a source in a given direction is the radiant flux leaving the source, propagated in an element of solid angle containing the given direction divided by that element of solid angle: $\Phi_e = \int I_e d\Omega$.	watt per steradian	W sr ⁻¹
The radiance L_e at a point of a surface and in a given direction (ϑ = angle between the direction and the normal to the surface) is the radiant intensity of an element of the surface divided by the area of the orthogonal projection of that element on a plane perpendicular to the given direction: $\Phi_e = \int I_e d\Omega = \iint L_e \cos \vartheta dA d\Omega$.	watt per steradian per square metre	W sr ⁻¹ m ⁻²
The radiant exitance M_e at a point of a surface element is the radiant flux leaving an element of the surface divided by the area of that element: $\Phi_e = \int M_e dA$.	watt per square metre	W m ⁻²
The irradiance E_e at a point of a surface is the radiant flux incident on an element of the surface divided by the area of that element: $\Phi_e = \int E_e dA$.	watt per square metre	W m ⁻²
The radiant exposure H_e is the time integral of the irradiance: $H_e = \int E_e dt$.	joule per square metre	J m ⁻²
The (hemispherical) emissivity of a thermal radiator ϵ is the ratio of the radiant exitance of the radiator to that of a black body at the same temperature: $\epsilon = M_e/M_{e,b}$ ***.	1	1
The spectral (hemispherical) emissivity of a thermal radiator $\epsilon(\lambda)$ is the ratio of the spectral concentration of the radiant exitance of the radiator to that of a black body at the same temperature: $\epsilon(\lambda) = M_{e,\lambda}/M_{e,\lambda,b}$ †.	1	1
The directional emissivity of a thermal radiator $\epsilon(\vartheta, \varphi)$ is the ratio of the radiance of the radiator in a given direction (ϑ, φ) to that of a black body at the same temperature: $\epsilon(\vartheta, \varphi) = L_e/L_{e,b} = \int \Phi_{e,\lambda} d\lambda / \int \Phi_{e,\lambda,b} d\lambda$.	1	1
The spectral directional emissivity of a thermal radiator $\epsilon(\lambda; \vartheta, \varphi)$ is the ratio of the spectral concentration of radiance in a given direction (ϑ, φ) of the radiator to that of a black body at the same temperature: $\epsilon(\lambda; \vartheta, \varphi) = L_{e,\lambda}/L_{e,\lambda,b} < 1$.	1	1
Light (luminous quantities)		
The luminous flux Φ_v is the radiant flux evaluated photometrically, i.e., by its action on a selective receptor. The spectral function for evaluating the spectral concentration of radiant flux $\Phi_{e,\lambda}$ is the spectral luminous efficacy $K(\lambda)$ or the spectral luminous efficiency $V(\lambda)$: $\Phi_v = \int K(\lambda) \Phi_{e,\lambda} d\lambda = K_{\max} \int V(\lambda) \Phi_{e,\lambda} d\lambda$.	lumen	lm = cd sr

* Where there is no risk of confusion between *radiant quantities* and the corresponding *luminous quantities* (i.e., the photometrically evaluated radiant quantities), or where the discussion concerns exclusively one of the two kinds of quantities, the subscripts of the symbols ('e' from 'energy', 'v' from 'visible') are omitted.

** Where there is no risk of confusion with the so-called 'spectral' quantities – for instance $\epsilon(\lambda)$, $K(\lambda)$, $V(\lambda)$, $e(\lambda)$, $\alpha(\lambda)$, $\tau(\lambda)$ – which though functions of wave length are nevertheless not spectral distribution functions in the sense of differential quotients with respect to wave length, the 'spectral concentration of a quantity X ' (i.e., $X_\lambda = dX/d\lambda$) may be des-

ignated shortly the 'spectral' quantity X . Thus the 'spectral concentration of radiant flux' ($\Phi_{e,\lambda}$) may be abbreviated to 'spectral radiant flux'.

*** $M_{e,b}$ is the unpolarized radiant exitance of a black body at the temperature T : $M_{e,b} = \sigma T^4$ (for the STEFAN-BOLTZMANN constant $\sigma = \pi^2 k^4/60 h^3 c^2$ see page 226).

† $M_{e,\lambda,b}$ is PLANCK's expression for the unpolarized spectral concentration of radiant exitance of a black body at the temperature T : $M_{e,\lambda,b} = c_1 \lambda^{-5} [\exp(c_2/\lambda T) - 1]^{-1}$ (for the 1st and 2nd PLANCK radiation constants, $c_1 = 2\pi^5 k^4/15 h^3 c^2$ and $c_2 = hc/k$, see page 228).

Quantity* and definition†	SI Unit	
	Name	Symbol
Light (concluded)		
The spectral reflectance $\rho(\lambda)$ is the ratio of the spectral concentration of the reflected radiant (or luminous) flux to that of the incident radiant (or luminous) flux: $\rho(\lambda) = \Phi_{\lambda r}/\Phi_{\lambda i}$.	1	1
The spectral absorptance $\alpha(\lambda)$ is the ratio of the spectral concentration of the absorbed radiant (or luminous) flux to that of the incident radiant (or luminous) flux: $\alpha(\lambda) = \Phi_{\lambda a}/\Phi_{\lambda i}$.	1	1
The spectral transmittance $\tau(\lambda)$ is the ratio of the spectral concentration of the transmitted radiant (or luminous) flux to that of the incident radiant (or luminous) flux: $\tau(\lambda) = \Phi_{\lambda tr}/\Phi_{\lambda i}$.	1	1
The reflectance ρ , absorptance α and transmittance τ are the respective ratios of the reflected, absorbed and transmitted radiant (or luminous) flux Φ_r , Φ_a and Φ_{tr} to the incident radiant (or luminous) flux Φ . The following relationships hold for the quantities ρ , α , τ and $\rho(\lambda)$, $\alpha(\lambda)$, $\tau(\lambda)$: $\rho = \int \Phi_{\lambda} \rho(\lambda) d\lambda / \int \Phi_{\lambda} d\lambda = \Phi_r / \Phi$ $\alpha = \int \Phi_{\lambda} \alpha(\lambda) d\lambda / \int \Phi_{\lambda} d\lambda = \Phi_a / \Phi$ $\tau = \int \Phi_{\lambda} \tau(\lambda) d\lambda / \int \Phi_{\lambda} d\lambda = \Phi_{tr} / \Phi$ $\Phi = \Phi_r + \Phi_a + \Phi_{tr}$ $\rho + \alpha + \tau = \rho(\lambda) + \alpha(\lambda) + \tau(\lambda) = 1$	1	1
<p>* See footnote *, page 222. ** For a thermal radiator emitting or absorbing in any direction (θ, φ): $\alpha(\lambda; \theta, \varphi) = \epsilon(\lambda; \theta, \varphi) = L_{e\lambda} / L_{e\lambda, s} < 1$.</p> <p>References † International Electrotechnical Commission, <i>International Lighting Vocabulary</i>, Draft 3rd ed. and amendments, Geneva, 1966 (unpublished); International Organization for Standardization, <i>Quantities and Units of Light and Related Electromagnetic Radiations</i>, Draft ISO Recommendation No. 1778, January 1969 (unpublished).</p> <p>2 Comité International des Poids et Mesures, <i>Proc.-Verb. Com.int. Poids Mes.</i>, 15, 65 (1933). 3 Comité International des Poids et Mesures, <i>Proc.-Verb. Com.int. Poids Mes.</i>, 20, 119 (1946), and 21, 67 (1948); Conférence Générale des Poids et Mesures, <i>Comptes rendus des séances de la 9^e Conférence générale des Poids et Mesures</i>, Paris 1948, Gauthier-Villars, Paris, 1949, page 54; <i>Comptes rendus des séances de la 13^e Conférence générale des Poids et Mesures</i>, Paris 1967/1968, Bureau International des Poids et Mesures, Sèvres, 1969, pages 71 and 104.</p>		

Quantity and definition†	Dimension	Units	
		SI unit	CGS unit
Acoustics †			
The sound pressure p is the alternating pressure due to an acoustical phenomenon and superimposed on the stationary atmospheric pressure. Values not otherwise specified are root mean square values, often called 'effective' values.	$L^{-1} M T^{-2}$	$N m^{-2}$	dyn cm^{-2} (= μbar)
The sound particle velocity v is the instantaneous velocity of a particle of the medium set in motion by an acoustical phenomenon. Values not otherwise specified are root mean square values, often called 'effective' values.	$L T^{-1}$	$m s^{-1}$	cm s^{-1}
The sound pressure level L_p is defined† as $20 \log_{10} (p/p_0)$ in decibel (dB), where p is the root mean square value of the measured sound pressure, and p_0 is the root mean square value of a reference pressure. For air: $p_0 = 2 \times 10^{-5} N m^{-2} = 2 \times 10^{-6} \mu\text{bar}$ is generally used†.	$L^0 M^0 T^0$	$\text{dB}^{\dagger\dagger}$	$\text{dB}^{\dagger\dagger}$
The sound energy W is the mechanical energy radiated as sound.	$L^2 M T^{-2}$	$W s$	erg
The sound power or sound energy flux P is the sound energy transferred in a certain time interval divided by the duration of that interval: $P = dW/dt$.	$L^2 M T^{-3}$	W	erg s^{-1}
<p>† This section (pages 224-226) has been compiled in collaboration with W. FURRER, Zurich.</p> <p>†† The decibel is not a unit of either the SI or the CGS system.</p>			

Acoustics

Quantity and definition [*]	Dimension	Units	
		SI unit	CGS unit
Acoustics (continued)			
The sound intensity I for unidirectional sound energy flux is the sound energy flux through an area normal to the direction of propagation divided by that area $P = I dA$.	$M T^{-2}$	$W m^{-2}$	$erg s^{-1} cm^{-2}$
The velocity of sound c is the velocity of propagation of a sound wave. It is a constant depending on the medium and independent of the frequency or intensity of the sound wave. The velocity of sound in air depends mainly on the temperature and is given by $c_{air} = (331.4 + 0.607 t) m s^{-1}$, where t is the numerical value of the temperature in degree Celsius. Note At very high intensities (explosions) the velocity of sound may be higher.	$L T^{-1}$	$m s^{-1}$	$cm s^{-1}$
	Dimension	SI unit	
The periodic time or period T is the time taken by a periodic phenomenon in an arbitrarily defined state to return for the first time to that state	T	s	
The frequency ν (or f) of a periodic phenomenon is the reciprocal of its periodic time. In acoustical phenomena the subjective impression of the pitch depends on the frequency. Standard musical pitch is the frequency for the note A in the treble staff, defined as 440 Hz.	T^{-1}	Hz	
The loudness level L_N (or A) of a sound or noise is expressed on the dimensionless phon scale ¹ . The loudness level amounts to π phon when it is judged by a normal observer under standardized listening conditions to be as loud as a pure tone of frequency 1000 Hz consisting of a plane progressive sound wave, coming from directly in front of the observer, the sound pressure level of which is $L_p = \pi$ dB (see above), i.e., $L_N = 20 \log_{10}(p/p_0)_{1000}$. In principle, therefore, loudness levels can be measured in phon only by a subjective hearing test, objective tests yield only more or less exact approximations.	$L^0 M^0 T^0$	phon*	
Loudness N (or S) Owing to the arbitrary definition of the decibel and phon scales, loudness levels on these scales do not immediately correspond to the sensation of loudness but have to be interpreted by the user on the basis of his personal experience of sounds of known phon value. The sone scale provides a means of expressing the subjective sensation of loudness and is defined ² by the following relationship between loudness N in sone and loudness level L_N in phon	$L^0 M^0 T^0$	sone*	

$$N = 2^{0.1(L_N - 40)} \text{ or } \log_{10} N = 0.1(L_N - 40) \quad \log_{10} 2 \approx 0.03 (L_N - 40)$$

Corresponding values of L_N and N calculated from this 'loudness function' are as follows

L_N in phon	N in sone	L_N in phon	N in sone	L_N in phon	N in sone
20	0.25	55	2.83	90	32.0
25	0.35	60	4.00	95	45.3
30	0.50	65	5.66	100	64.0
35	0.70	70	8.00	105	90.5
40	1.00	75	11.3	110	128
45	1.41	80	16.0	115	181
50	2.00	85	22.6	120	256

* Not an SI unit

It should be noted that

- 1 Loudness in sone cannot be measured directly but must be calculated from the loudness level in phon.
- 2 A loudness of 1 sone corresponds to a loudness level of 40 phon
- 3 A twofold change in loudness corresponds to a loudness level difference of 10 phon
- 4 The relationship has been confirmed experimentally only between 20 and 120 phon, outside this range its use must be regarded as an extrapolation

Calculation of loudness levels

Loudness levels can also be calculated from noise analyses, the two best-known methods being those of STEVENS³ and ZWICKER⁴.

as 'perceived noise levels' (PN) and are expressed in decibel. They represent a degree of correlation of objective measurements with subjective sensation not attainable simply by measuring sound pressure levels

Sound level meters

In view of the complexity of the human ear and the difficulty of the subjective hearing tests required for the measurement of loudness levels in phon, sound level meters measuring certain weighted sound pressure levels have been standardized⁵. The weighting applied to each sinusoidal component of the sound pressure

by a particular method

A modification of STEVENS' method has been introduced for the measurement of aircraft noise⁶. The values so obtained are known

sure is given as a function of frequency by three standard reference curves A, B and C. The varying sensitivity of the ear is taken into account by using curve A for low sound pressure levels, curve B for moderate sound pressure levels, and curve C for high sound pressure levels. In each measurement the curve used must be shown, for instance by placing the appropriate letter after the decibel value: 45 dB(A), 95 dB(C). The 'DIN-phon' earlier used in Germany⁷ was based on the same principle.

More recent measurements of the frequency response of the ear⁸ and studies of the correlation between sound pressure level and loudness level measurements have shown that the use of the curve A gives best agreement with the subjective sensation and that this applies not only to low but also to high sound pressure levels. This is being taken into account by the ISO when standardizing in this field, with the result that the tendency is now for sound levels to be measured and given in dB(A). Sound pressure levels in dB(A) should also be given when loudness levels are measured or calculated in any form (for instance L_N in phon or in phon by STEVENS' method, PN in dB, etc.).

Typical sound levels

The following examples from everyday life illustrate the range of the dB(A) sound level scale:

Source	Sound level in dB(A)
Propeller aircraft at 5 m	130
Pneumatic hammer at 1 m	120
Brass foundry	110
Motor-car horn at 5 m	100
Truck at 5 m	90
Loud radio music	80
Normal conversation at 1 m	70
Motor car at 10 m	60
Quiet stream or river	50
Residential district without traffic	40
Quiet garden	30
Ticking of a watch	20
Limit of audible noise	10
Absolute silence	0

References

1. International Organization for Standardization, *Expression of the Physical and Subjective Quantities in Acoustics*, ISO Recommendation R131, September 1955.
2. STEVENS, S.S., *J. Acoust. Soc. Amer.*, **28**, 807 (1956).
3. ZWICKER, E., *Acustica*, **10**, 304 (1960).
4. KRYTER and PEARSONS, *J. Acoust. Soc. Amer.*, **35**, 866 (1963).
5. International Electrotechnical Commission, *Recommendations for Sound Level Meters*, Publication 123, and *Precision Sound Level Meters*, Publication 179, Bureau central de la Commission électrotechnique internationale, Geneva, 1961 and 1965.
6. Deutscher Normenausschuß (DNA), *Meßgerät für DIN-Lautstärken*, DIN 5045, May 1963, Beuth-Vertrieb, Berlin, 1963 (superseded by *Präzisions-schallpegelmessung, Allgemeine Anforderungen*, DIN 45633, Blatt 1, July 1967, Beuth-Vertrieb, Berlin, 1967).
7. International Organization for Standardization, *Preferred Frequencies for Acoustical Measurements*, ISO Recommendation R266, August 1962.

Amount of substance

Amount of substance (n) and amount of equivalent (n_{eq})

Dimension = N

(Additional*) base unit = mole (mol)

Except in special cases, there is no practicable method of counting the numbers of particles involved in a chemical or physical process. This is the reason the IUPAC^{1,2} in 1957 introduced the basic quantity 'amount of substance' n for use in chemical and molecular physics. The concept of amount of substance is founded on the 'countability' of

identical individuals (particles) in an atomic or other discontinuous system². The value of n is proportional to the number of particles N , the proportionality factor being a fundamental constant, the Avogadro constant (see also page 228) $N_A \approx N/n$ (dimension = N^{-1}). The number of particles in a population having the amount of substance $n = 1 \text{ mol}$ is therefore $N = N_A \times 1 \text{ mol} = 6.022 \times 10^{23}$.

The base unit of amount of substance is the mole* (mol). The primary standard for the mole – as well as for the scale of relative atomic masses A_r and the (unified) atomic mass unit (u) – is the carbon nuclide ^{12}C on which the IUPAC and IUPAP agreed in 1960–61^{3,4}. As defined by the IUPAC^{6, **}, the mole is the amount of substance of a system which contains as many elementary units as there are carbon atoms in 0.012 kg of the pure nuclide carbon-12 (^{12}C). The elementary unit must be specified and may be an atom, a molecule, an ion, an electron, a photon, etc., or a specified group of such entities.

The concept of amount of substance may be extended to FARADAY'S law of equivalence and chemical bonds. Here use is made of the amount of equivalent n_{eq} (dimension likewise N): $n_{\text{eq}} = z n$, where z is the charge number in the case of ions and the number (single, double, etc.) in the case of bonds. The amount of equivalent n_{eq} is proportional to the electric charge $Q = N z e$ (e = elementary charge; see also page 228) of N ions of charge number z , the proportionality factor again being a fundamental constant, the FARADAY constant F (see also page 228) $= Q/n_{\text{eq}} = e N/n = e N_A$ (dimension = C mol^{-1}). The unit of amount of equivalent is likewise the base unit mole*. The electric charge carried by the amount of equivalent $n_{\text{eq}} = z n = 1 \text{ mole}$ of a particular species of ion is therefore $Q = F n_{\text{eq}} = F \times 1 \text{ mol} = 9.6487 \times 10^4 \text{ C}$.

Scale of relative atomic masses (A_r) and the (unified) atomic mass unit (u)

The unified scale of relative atomic masses A_r , with ^{12}C as reference nuclide or primary standard, is defined^{3,4} by the assigned value

$$A_r(^{12}\text{C}) = 12$$

Using the mass $m(^{12}\text{C})$ of an atom of the nuclide ^{12}C as primary standard, the (unified) atomic mass unit (u) is defined by the relation³

$$1 u = m(^{12}\text{C})/12$$

The atomic mass of any nuclide X can therefore be written^{2,5} $m(X) = A_r(X) u$ with

$$1 u = 10^{-3} (N_A \text{ mol}^{-1})^{-1} \text{ kg} = 1.66053 \times 10^{-27} \text{ kg}$$

Tables of the relative atomic masses $m(X)$ of the nuclides have been published at the instance of the Commission on Atomic Masses and Related Atomic Constants of the IUPAP^{9, 10}. These data, together with the 'natural' or 'average' relative abundancies of the stable isotopes of the elements, have formed since 1961 the basis of the tables of 'atomic weights' of the elements issued by the Commission on Atomic Weights of the IUPAC¹¹.

* Previously the mole, defined as $1 \text{ mol} = M_r g$ (M_r = relative molecular mass, or 'molecular weight', of the substance concerned), has been used as an individual (chemical) mass unit². Linked to the mole there is a further individual (electrochemical) mass unit for ions of a chemically homogeneous substance, the gramme-equivalent E_q , defined by $1 E_q = (1/z) \text{ mol} = (M_r/z) g$ (the symbol val is also used in place of E_q). The ratio M_r/z is known as the dimensional weight of the ions. These units have now been superseded by the dimensionless quantity amount of equivalent ($n_{\text{eq}} = z n$), i.e., the terms amount of equivalent $n_{\text{eq}} = y \text{ mol}$ and amount of substance $n = (y/z) \text{ mol}$ of the ions in the new formulation replace the earlier statement of a 'mass $y E_q$ of ions of molecular weight M_r and electrovalency z '.

At the instigation of the IUPAC, IUPAP and ISO, the Advisory Committee on Units in 1967 recommended⁸ to the International Committee of Weights and Measures that the International System of Units should be extended to include a seventh base unit, the mole, as base unit of amount of substance. The 13th General Conference of Weights and Measures in 1967 deferred a decision on this proposal. This recommendation was confirmed¹² by the Advisory Committee on Units in 1969.

Editors' note: In view of the fact that in clinical chemistry the equivalent, milliequivalent, etc., continue for the time being to be used as mass units¹³, the editors have refrained from making corresponding changes in the data given in subsequent chapters of these *Scientific Tables*.

** The same definition of the mole has been agreed upon by the ISO⁷ and IUPAC⁵, except that the latter has chosen a slightly different wording.

quantities representing concentration

Quantity*	Symbol and definition	mol-St units*
Molecular concentration of the component i (L^{-3})	$C_i = N_i/V$ (in a mixture of volume V)	m^{-3}
Mass concentration of the component i ($\text{L}^{-3} \text{M}$)	$\varrho_i = \bar{m}_i/V$ (in a mixture of volume V) (\bar{m}_i = mass of component i)	kg m^{-3}
Molarity of the component i ($\text{L}^{-3} \text{N}$)	$c_i = n_i/V$ (amount of substance in mol related to the volume of the mixture or solution)***	mol m^{-3}
Molality of the solute substance i ($\text{M}^{-1} \text{N}$)	$m_i = n_i/\bar{m}_0$ (amount of substance in mol related to the mass \bar{m}_0 of the solvent)***	mol kg^{-1}
Equivalent concentration of the ion i ($\text{L}^{-3} \text{N}$)	$c_{\text{eq}, i} = z_i c_i = z_i n_i/V$ (in a solution of volume V)***	mol m^{-3}
Ionic strength of a solution ($\text{M}^{-1} \text{N}$)	$I = \frac{1}{2} \sum_i z_i^2 m_i = \frac{1}{2} \sum_i z_i^2 c_i \bar{m}_0$ (\bar{m}_0 = mass of solvent)	mol kg^{-1}

* Dimensions in brackets

** Coherent unit in the International System of Units supplemented by the base unit mole (see above and reference*)

*** A solution of molarity $c_i = y \text{ mol/l}$ is known as 'y-molar' with respect to the component i , a solution of molality $m_i = y \text{ mol/kg}$ as 'y-molal' with respect to the component i , a solution of equivalent concentration $c_{\text{eq}, i} = y \text{ mol/l}$ as 'y-normal' with respect to the ions of species i .

Quantities related to amount of substance

Apart from amount of substance n , a number of other quantities

are used to describe the state of a system, e.g. pressure p , temperature T , and R ($\text{L}^2 \text{M}^{-1} \text{T}^{-2} \text{K}^{-1} \text{N}^{-1}$).

In analogy with the quantities related to amount of substance the equivalent conductivity Λ ($\text{L}^{-2} \text{M}^{-1} \text{T}^2 \text{N}^{-1}$) has, for instance, been introduced as the conductivity γ related to the equivalent concentration c_{eq} : $\gamma = \Lambda c_{\text{eq}}$ (γ = volume of the solution) $\Lambda = \gamma/c_{\text{eq}}$.

Earlier 'physical' (A_{ph}) and 'chemical' (A_{ch}) scales of atomic weights

Before agreement was reached on the unified ^{12}C scale, different relative mass scales² were in use in physics and chemistry², namely the 'physical scale of atomic weights' based on the oxygen nuclide ^{16}O as primary standard and defined by $A_{\text{ph}}(^{16}\text{O}) = 16$, and the 'chemical scale of atomic weights' based on elementary oxygen, i.e., on the 'mean atomic weight' $\bar{A}_{\text{ch}}(^{16}\text{O}) = 16$.

and between the three corresponding units of amount of substance mol ($^{16}\text{O} = 16$), mol ($\bar{\text{O}} = 16$) and mol ($^{12}\text{C} = 12$)

$$\frac{A_{\text{ph}}(^{16}\text{O} = 16)}{A_{\text{ch}}(^{16}\text{O} = 16)} = \frac{\text{mol}(^{16}\text{O} = 16)}{\text{mol}(\bar{\text{O}} = 16)} = 1.00031791^{10}$$

$$\frac{A_{\text{ph}}(^{16}\text{O} = 16)}{A_{\text{ch}}(^{12}\text{C} = 12)} = \frac{\text{mol}(^{16}\text{O} = 16)}{\text{mol}(^{12}\text{C} = 12)} = 1.000318$$

$$\frac{A_{\text{ph}}(^{16}\text{O} = 16)}{A_{\text{ch}}(^{12}\text{C} = 12)} = \frac{\text{mol}(\bar{\text{O}} = 16)}{\text{mol}(^{12}\text{C} = 12)} = \frac{1.000318}{k_A} = 1.00043$$

Former atomic mass unit (amu)

The former atomic mass unit (amu), based on the oxygen nuclide ^{16}O as primary standard and linked to the physical scale of atomic weights², was defined through the mass $m(^{16}\text{O})$ of an atom of the nuclide ^{16}O

$$1 \text{ amu} = m(^{16}\text{O})/16$$

The atomic mass of any nuclide X was therefore written as $m(X) = A_{\text{ph}}(X) \text{ amu}$. The relationship between the earlier and the present unified atomic mass unit is given by

$$1 \text{ u} = \frac{A_{\text{ch}}(^{16}\text{O} = 16)}{A_{\text{ch}}(^{12}\text{C} = 12)} \text{ amu}$$

Re

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¹⁰ Comité consultatif des unités, 3^{re} session, Paris, 1967, p. 10.
¹¹ Comité consultatif des unités, 2^e session, Paris 1959 (in p. 6).
¹² Everling et al., *Nuclear Phys.* 18, 529 (1960), König et al. *ibid.* 31, 18 (1962).

¹³ International Union of Pure and Applied Chemistry, *Comptes rendus de la 17^e assemblée*, Stockholm 1953, Butterworth, London, page 93, *Comptes rendus de la 18^e assemblée*, Zurich 1955, Butterworth, London, page 115.

¹⁴ International Union of Pure and Applied Chemistry, *Comptes rendus de la 17^e assemblée*, Stockholm 1953, Butterworth, London, page 93, *Comptes rendus de la 18^e assemblée*, Zurich 1955, Butterworth, London, page 115.

Physical Constants¹

	Symbol and formula	Numerical value	CGS system	International System of Units	Noncoherent units
Gravitational constant ¹	G	6.670 ± 0.015	$10^{-8} \text{ dyn cm}^2 \text{ g}^{-2}$	$10^{-11} \text{ N m}^2 \text{ kg}^{-2}$	

Electromagnetic field constants (see also page 215)

Velocity of light in vacuum ¹	c	2.997 925	$10^{10} \text{ cm s}^{-1}$	10^8 m s^{-1}	
	$1/c$	3.335 640 5	$10^{-11} \text{ cm}^{-1} \text{ s}$	$10^{-9} \text{ m}^{-1} \text{ s}$	
	c^2	8.987 554 3	$10^{20} \text{ cm}^2 \text{ s}^{-2}$	$10^{16} \text{ m}^2 \text{ s}^{-2}$	
	$1/c^2$	1.112 649 7	$10^{-21} \text{ cm}^{-2} \text{ s}^2$	$10^{-17} \text{ m}^{-2} \text{ s}^2$	
Magnetic field constant	$\mu_0 = 4\pi \cdot 10^{-7} \text{ H m}^{-1}$	1.256 637 061		10^{-6} H m^{-1}	
Electric field constant	$\epsilon_0 = 1/\mu_0 c^2$	8.854 185 3		$10^{-12} \text{ F m}^{-1}$	
Impedance of vacuum	$\Gamma_0 = \mu_0 c$	3.767 303 7		$10^2 \Omega$	

Thermodynamic constants¹⁻⁴

Molar volume of an ideal gas under standard conditions	V_{m0}	2.241 36	$10^4 \text{ cm}^3 \text{ mol}^{-1}$	$10^{-2} \text{ m}^3 \text{ mol}^{-1}$	
Molar gas constant	$R = p_0 V_{m0}/T_0$	8.314 3 8.205 6 1.987 2 1.986 5 1.985 8	$10^7 \text{ erg K}^{-1} \text{ mol}^{-1}$	$\text{J K}^{-1} \text{ mol}^{-1}$	$10 \text{ cm}^3 \text{ atm K}^{-1} \text{ mol}^{-1}$ $\text{cal}_{18} \text{ K}^{-1} \text{ mol}^{-1}$ $\text{cal}_{15} \text{ K}^{-1} \text{ mol}^{-1}$ $\text{cal}_{IT} \text{ K}^{-1} \text{ mol}^{-1}$

Atomic constants¹⁻⁴

AVOGADRO constant ^{1††}	N_A	6.022 2	10^{23} mol^{-1}	10^{23} mol^{-1}	
LOSCHMIDT constant ^{1†††}	$n_L = N_A/V_{m0}$	2.686 8	10^{19} cm^{-3}	10^{23} m^{-3}	
BOLTZMANN entropy constant	$k = R/N_A$	1.380 6 1.362 6 8.617 1 3.299 8 3.298 6 3.297 6	$10^{-16} \text{ erg K}^{-1}$	$10^{-23} \text{ J K}^{-1}$	$10^{-22} \text{ cm}^3 \text{ atm K}^{-1}$ $10^{-5} \text{ eV K}^{-1}$ $10^{-24} \text{ cal}_{18} \text{ K}^{-1}$ $10^{-24} \text{ cal}_{15} \text{ K}^{-1}$ $10^{-24} \text{ cal}_{IT} \text{ K}^{-1}$
Elementary charge	e e^* e^*/e	1.602 2 4.803 2 1.602 2	10^{-10} esu 10^{-20} emu	10^{-19} C	
FARADAY constant	$F = N_A e$ $F^* = N_A e^*$ $F^*/e = N_A e^*/e$	9.648 7 2.892 6 9.648 7	$10^{14} \text{ esu mol}^{-1}$ $10^3 \text{ emu mol}^{-1}$	10^4 C mol^{-1}	
SOMMERFELD fine-structure constant ..	α $1/\alpha$ α^2	7.297 35 1.370 36 5.325 1	10^{-3} 10^2 10^{-5}	10^{-3} 10^2 10^{-5}	
PLANCK constant (quantum of action) ..	$h = 2\pi (e^*)^2/\alpha e$ h/e^* h/e^* h/e	6.626 2 1.379 52 4.135 71	10^{-27} erg s $10^{-17} \text{ erg s esu}^{-1}$ $10^{-7} \text{ erg s emu}^{-1}$	10^{-34} J s	
Quantum-mechanical unit of angular momentum	$h = h/2\pi$	1.054 59	10^{-27} erg s	10^{-34} J s	
1st PLANCK radiation constant	$c_1 = 2\pi h c^2$ $h c^2$	3.741 8 5.955 3	$10^{-5} \text{ erg cm}^2 \text{ s}^{-1}$ $10^{-6} \text{ erg cm}^2 \text{ s}^{-1}$	10^{-16} W m^2 10^{-17} W m^2	
2nd PLANCK radiation constant	$c_2 = h c/k$ $c_2/c = h/k$	1.438 8 4.799 4	cm K 10^{-11} s K	10^{-2} m K 10^{-11} s K	
Constant of WIEN's displacement law ..	$b = \lambda_{\text{max}} T = c_2/x$ $x = 4.965 114 23$	2.897 9	10^{-1} cm K	10^{-3} m K	
STEFAN-BOLTZMANN constant	$\sigma = \pi^2 k^4/60 h^3 c^2$	5.669 6	$10^{-5} \text{ erg cm}^{-2} \text{ s}^{-1} \text{ K}^{-4}$	$10^{-8} \text{ W m}^{-2} \text{ K}^{-4}$	
BOHR radius (of the first-quantized electron orbit of the hydrogen atom) ..	$a_0 = \alpha/4\pi R_\infty$	5.291 77	10^{-9} cm	10^{-11} m	

¹ The data on the physical constants (pages 228 and 229) have been compiled in collaboration with E. R. COHEN, North American Aviation Science Center, Thousand Oaks, Calif., USA. The values given are corrected from a consistent set derived by the Committee on Fundamental Constants of the National Academy of Sciences - National Research Council (USA)^{1,2}. The original set was approved by the International Union of Pure and Applied Physics at the 12th General Assembly in 1963³ and published in 1965⁴. The numerical values given here correct these data to reflect a change of 20 ppm in the value of the Sommerfeld fine-structure constant. This change has been made necessary by recent measurements of the macroscopic quantities in superconductors and on the fine structure in the

The quantities elementary charge, FARADAY constant, gyromagnetic ratio and magnetic moment, defined non-rationally in the symmetrical three-dimensional system of quantities, are given the symbols e^* , F^* , γ^* and μ^* , the corresponding quantities defined rationally in the four-dimensional system have the symbols e , F , γ and μ ; $e^*/e = F^*/F = (4\pi\epsilon_0)^{-1/2}$, $\gamma^*/\gamma = \mu^*/\mu = (\mu_0/4\pi)^{1/2}$ (see 'Electricity and Magnetism', page 215).

^{††} The molar number of molecules (see 'Quantities related to amount of substance', page 227). Formerly known as the LOSCHMIDT constant in German-speaking countries.

^{†††} The number density of molecules of an ideal gas at 0 °C and 760 torr. Formerly known as the AVOGADRO constant in German-speaking countries.

	Symbol and formula	Numerical value	CGS system	International System of Units	Noncoherent units
Atomic constants (continued)					
Electron radius	$r_e = \alpha^2/4\pi R_\infty$	2 817 94	10^{-12} cm	10^{-15} m	
Thomson cross-section	$(8\pi/3)r_e^2$	6 652 5	10^{-28} cm ²	10^{-28} m ²	10^{-1} barn
Compton wave length of electron	$\lambda_{Ce} = h/m_e c$	2 425 31	10^{-10} cm	10^{-10} m	
	$\lambda_{Ce}/2\pi$	3 861 59	10^{-11} cm	10^{-11} m	
	$\lambda_{Cp} = h/m_p c$	1 321 44	10^{-15} cm	10^{-14} m	
	$\lambda_{Cn}/2\pi$	2 103 14	10^{-15} cm	10^{-14} m	
of proton	$\lambda_{Cp} = h/m_p c$	1 319 62	10^{-15} cm	10^{-14} m	
	$\lambda_{Cn}/2\pi$	2 100 24	10^{-15} cm	10^{-14} m	
of neutron	$\lambda_{Cn} = h/m_n c$				
	$\lambda_{Cn}/2\pi$				
Rydberg constant for an atom with a nucleus of infinite mass	R_∞	1 097 373 1	10^5 cm ⁻¹	10^7 m ⁻¹	
for ¹ H atom	$R_H = R_\infty / (1 + m_e/m_p)$	1 096 775 8	10^5 cm ⁻¹	10^7 m ⁻¹	
Rydberg frequency for an atom with a nucleus of infinite mass	$R_\infty^f = R_\infty c$	3 289 842	10^{11} s ⁻¹	10^{13} s ⁻¹	
for ¹ H atom	$R_H^f = R_H c$	3 286 052	10^{11} s ⁻¹	10^{13} s ⁻¹	
Charge to mass ratio for positron	e/m_e	1 758 80		10^{11} C kg ⁻¹	
	e^2/m_e	5 272 76	10^{19} esu g ⁻¹		
	$e^2/m_e c$	1 758 80	10^7 esu g ⁻¹		
Charge to mass ratio for proton	e/m_p	9 579 00		10^7 C kg ⁻¹	
	e^2/m_p	2 871 72	10^{14} esu g ⁻¹		
	$e^2/m_p c$	9 579 00	10^8 esu g ⁻¹		
Gyromagnetic ratio of proton	γ_p^0	2 675 19	10^4 s ⁻¹ emu ⁻¹	10^8 s ⁻¹ T ⁻¹	
	γ_p^1				
Effective gyromagnetic ratio of proton in a spherical sample of water (uncorrected for diamagnetism in water sample)	γ_p^2	2 675 13	10^4 s ⁻¹ emu ⁻¹	10^8 s ⁻¹ T ⁻¹	
	γ_p^3				
Bohr magneton	$\mu_B^0 = h e^2/2 m_e c$	9 274 1	10^{-21} erg emu ⁻¹	10^{-24} J T ⁻¹	
	$\mu_B = h e^2/2 m_e$				
Nuclear magneton	$\mu_N^0 = (m_e/m_p)\mu_B^0$	5 051 0	10^{-24} erg emu ⁻¹	10^{-27} J T ⁻¹	
	$\mu_N = (m_e/m_p)\mu_B$				
Magnetic moment of electron	$\mu_e^0 = \mu_B^0 (g_e^0/2)$	9 284 9	10^{-21} erg emu ⁻¹	10^{-24} J T ⁻¹	
	$\mu_e = \mu_B (g_e/2)$				
Magnetic moment of proton	$\mu_p^0/\mu_N^0 = \mu_p^0/\mu_N$	1 001 159 64			
	$\mu_p^0 = \mu_N^0 (g_p^0/2)$				
	$\mu_p = \mu_N (g_p/2)$				
	$\mu_p^0/\mu_N^0 = \mu_p/\mu_N$				
Effective magnetic moment of proton in a spherical sample of water	$\mu_p^2/\mu_N^2 = \mu_p^2/\mu_N^2$	1 410 6	10^{-21} erg emu ⁻¹	10^{-24} J T ⁻¹	
	$\mu_p^2 = \mu_N^2 (g_p^2/2)$				
	$\mu_p^2/\mu_N^2 = \mu_p^2/\mu_N^2$	1 521 033	10^{-21}	10^{-24}	
	$\mu_p^2/\mu_N^2 = \mu_p^2/\mu_N^2$	2 792 78			
Zeeman splitting constant	$\mu_B^0/\mu_N^0 = \mu_B^0/\mu_N$	2 792 71			
	$\mu_B^0/\mu_N^0 = \mu_B^0/\mu_N$				
Atomic mass constant	$m_u = (1/N_A) g \text{ mol}^{-1}$	1 660 53	10^{-24} g	10^{-27} kg	u
	$m_u = (1/12) m(^{12}\text{C})$	1			
Rest mass of electron†	$m_e = 4\pi(e^2/c^2) R_\infty/\alpha^2$	9 109 6	10^{-32} g	10^{-31} kg	10^{-6} u
	$= e^2 R_\infty / (2\pi\alpha^2 c^2)$	5 485 93			
Rest mass of proton†	$m_p = m(^{1}\text{H}) - m_e$	1 672 62	10^{-24} g	10^{-27} kg	u
		1 007 276 61			
Ratio of the rest masses of proton and electron	m_p/m_e	1 836 1	10^3	10^3	
Rest mass of neutron†	$m_n = A_{rn} m_u$	1 674 92	10^{-24} g	10^{-27} kg	u
		1 608 665 20			
Rest mass of ¹ H atom†	$m(^1\text{H}) = A_r(^1\text{H}) m_u$	1 673 52	10^{-24} g	10^{-27} kg	u
		1 007 825 2			
Reduced mass of electron in ¹ H atom	$\mu = m_e m_p / m(^1\text{H})$	9 104 6	10^{-32} g	10^{-31} kg	10^{-6} u
		5 482 94			
Energy equivalents††					
	Atomic mass unit	$E(u) = c^2 \times (1 \text{ u})$	1 492 411	10^{-10} J	10^8 eV
			9 314 81		
Electron mass	$E(m_e) = c^2 m_e$	8 187 26	10^{-9} erg	10^{-14} J	10^6 eV
		5 110 04			
Proton mass	$E(m_p) = c^2 m_p$	1 503 27	10^{-8} erg	10^{-13} J	10^9 eV
		9 382 60			
Neutron mass	$E(m_n) = c^2 m_n$	1 505 34	10^{-8} erg	10^{-13} J	10^9 eV
		9 395 53			

† Relative atomic masses (A_r) (formerly 'atomic weights') of electron, proton, neutron and ¹H atom = numerical value \times power of ten of the appropriate rest mass measured in the atomic mass unit u (dimensionless)

†† For other energy equivalents see page 213

References

† National Academy of Sciences - National Research Council Committee, *Nat Bur Stand., Tech Note Bull.*, 47, 175 (1963)

Standard substances

Mercury

Density under standard conditions¹ (0 °C, 760 torr):

$$\rho_{\text{Hg}} = 13.59508 \text{ kg dm}^{-3}$$

The mean density of pure mercury at the temperature t_{Hg} in a barometric column supported by the pressure p being measured is given, with sufficient accuracy over the temperature range from 0 °C to 40 °C and for the pressures relevant to the IPTS-68 (see page 209), by the relation²

$$\rho(t_{\text{Hg}}, \frac{p}{2}) = \frac{\rho(20^\circ\text{C}, p_0)}{[1 + A(t_{\text{Hg}} - 20^\circ\text{C}) + B(t_{\text{Hg}} - 20^\circ\text{C})^2] \cdot [1 - \kappa(\frac{p}{2} - p_0)]}$$

where $A = 18.115 \times 10^{-8} \text{ }^\circ\text{C}^{-1}$; $B = 0.8 \times 10^{-8} \text{ }^\circ\text{C}^{-2}$; compressibility $\kappa = 4 \times 10^{-11} \text{ N}^{-1} \text{ m}^2$; $\rho(20^\circ\text{C}, p_0) = 13.54587 \text{ kg/m}^3$.

Relative density with density of water as reference quantity ('specific gravity'):

$$d(\text{Hg}) = \rho_{\text{Hg}}(1\text{g})/\rho_{\text{max}}(\text{H}_2\text{O}) = 13.59546$$

Water

Maximum density³ ($\approx 3.98^\circ\text{C}$, 760 torr, air-free):

$$\rho_{\text{max}}(\text{H}_2\text{O}) = (0.999972 \pm 0.000003) \text{ kg dm}^{-3}$$

Density between 0 and 40 °C in kg dm^{-3} (760 torr, air-saturated)⁴

°C	°C	°C	°C	°C	°C	°C	°C	°C	°C
0	0.999840	3	0.999964	6	0.999940	9	0.999781	12	0.999498
1	0.999899	4	0.999972	7	0.999902	10	0.999700	13	0.999378
2	0.999940	5	0.999964	8	0.999849	11	0.999606	14	0.999245

°C	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
15	0.999101	085	070	055	039	024	008	992	976	960
16	0.998944	928	911	895	878	862	845	828	811	793
17	0.998776	759	741	724	706	688	670	652	634	615
18	0.998597	578	560	541	522	503	484	465	446	426
19	0.998407	387	367	347	328	308	287	267	247	226
20	0.998206	185	164	143	122	101	080	059	037	016
21	0.997994	972	951	929	907	885	862	840	818	795
22	0.997772	750	727	704	681	658	634	611	588	564
23	0.997540	517	493	469	445	421	397	372	348	323
24	0.997299	274	249	224	199	174	149	124	098	073
25	0.997048	021	996	970	944	918	892	865	839	813

°C	°C	°C	°C	°C	°C
26	0.996786	29	0.995948	32	0.995030
27	0.996516	30	0.995650	33	0.994707
28	0.996236	31	0.995344	34	0.994375
				35	0.994036
				36	0.993688
				37	0.993333
				38	0.992969
				39	0.992598
				40	0.992220

Density of heavy water (100% D₂O, 760 torr, air-free)

°C	kg dm ⁻³	Reference	°C	kg dm ⁻³	Reference
3.8	1.10530	4a	20	1.10524	4a
5	1.10546	4a	25	1.10434	6
10	1.10585	4a	30	1.10312	6
11.23	1.10593*	5	35	1.10164	6
15	1.10574	4a	40	1.09986	6

* Maximum density.

Specific heat capacity of water between 0 and 100 °C (at 760 torr)⁷

J g ⁻¹ K ⁻¹										
°C	0	1	2	3	4	5	6	7	8	9
0	4.2174	4.2138	4.2104	4.2074	4.2048	4.2019	4.1996	4.1974	4.1954	4.1936
10	4.1919	4.1904	4.1890	4.1877	4.1866	4.1855	4.1846	4.1837	4.1829	4.1822
20	4.1816	4.1810	4.1805	4.1801	4.1797	4.1793	4.1790	4.1787	4.1785	4.1783
30	4.1782	4.1781	4.1780	4.1780	4.1779	4.1779	4.1780	4.1780	4.1781	4.1782
40	4.1783	4.1784	4.1786	4.1788	4.1789	4.1792	4.1794	4.1796	4.1799	4.1801
50	4.1804	4.1807	4.1811	4.1814	4.1817	4.1821	4.1825	4.1829	4.1833	4.1837
60	4.1841	4.1846	4.1850	4.1855	4.1860	4.1865	4.1871	4.1876	4.1882	4.1887
70	4.1893	4.1899	4.1905	4.1912	4.1918	4.1925	4.1932	4.1939	4.1946	4.1954
80	4.1961	4.1969	4.1977	4.1985	4.1994	4.2002	4.2011	4.2020	4.2029	4.2039
90	4.2048	4.2058	4.2068	4.2078	4.2089	4.2100	4.2111	4.2122	4.2133	4.2145
100	4.2156									

cal₁₈ g⁻¹ K⁻¹ (calculated by the editors from the CIPM values)⁷

°C	0	1	2	3	4	5	6	7	8	9
0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
10	0.00762	0.00676	0.00595	0.00523	0.00454	0.00392	0.00337	0.00284	0.00237	0.00194
20	0.00153	0.00117	0.00084	0.00053	0.00026	0.00000	99978	99957	99938	99921
30	99907	99892	99881	99871	99861	99852	99845	99838	99833	99828
40	99826	99823	99821	99820	99818	99818	99821	99821	99823	99826
50	99828	99830	99835	99840	99842	99849	99854	99859	99866	99871
60	99878	99885	99895	99902	99909	99919	99928	99938	99947	99957
70	99967	99978	99988	99998	100000	100024	100038	100050	100065	100076
80	100091	100105	100119	100136	100151	100167	100184	100201	100217	100237
90	100253	100272	100291	100311	100332	100351	100373	100394	100416	100440
100	100461	100485	100509	100533	100559	100585	100612	100638	100664	100693

For the triple and boiling points of water and melting point of ice see page 20 for the vapour pressure of water see pages 256–258.

Viscosity of water between 0 and 40 °C⁸

Temperature / in °C	Viscosity ratio $\eta/\eta_{20^\circ\text{C}}$	Dynamic viscosity η in cP	Kinematic viscosity ν in cSt
0	1.7885	1.792	1.792
5	1.5170	1.520	1.520
10	1.3043	1.3069	1.3073
15	1.1360	1.1383	1.1393
20	1.0000	1.0020	1.0038
25	0.8885	0.8903	0.8929
30	0.7959	0.7975	0.8010
35	0.7179	0.7193	0.7236
40	0.6518	0.6531	0.6582

Air

Standard density of dry air free of carbon dioxide (0 °C, 760 torr)⁹:

$$\rho_{\text{air}} = 1.2928 \times 10^{-3} \text{ kg dm}^{-3}$$

Standard conditions for air in spectroscopy:

760 torr, 15 °C, 0.03% CO₂, dry

Acceleration due to gravity

Standard acceleration due to gravity¹⁰:

$$g_{\text{N}} = 980.665 \text{ Gal (cm s}^{-2}\text{)}$$

International gravity formula¹¹ (based on the international terrestrial ellipsoid):

$$y_0 = (980.632272 - 2.586145 \cos 2B + 0.002878 \cos 4B - 0.000004 \cos 6B) \text{ Gal}$$

where y_0 = acceleration due to gravity at sea level, B = latitude. This yields the following values for different degrees of latitude (calculated by the editors):

Latitude in °	y_0 in Gal	y_0/g_{N}	g_{N}/y_0	Latitude in °	y_0 in Gal	y_0/g_{N}	g_{N}/y_0
0	978.0490	0.997332	1.002675	45	980.6294	0.999964	1.000036
5	0881	372	635	46	7197	1.000056	0.999944
10	2043	491	516	47	8098	148	852
15	3940	684	321	48	8998	239	761
20	6517	947	057	49	9894	331	669
25	9694	0.998271	1.001732	50	981.0787	422	578
30	979.3378	647	355	51	1673	512	458
31	4165	727	275	52	2554	602	398
32	4968	809	193	53	3427	691	309
33	5785	892	109	54	4291	779	221
34	6614	977	025	55	5146	866	134
35	7456	0.999062	1.000938	56	5990	952	048
36	8308	149	851	57	6822	1.001037	0.998963
37	9170	237	763	58	7642	121	820
38	980.0041	326	674	59	8448	203	738
39	0920	416	585	60	9239	284	718
40	1805	506	494	65	982.2941	661	342
41	2696	597	403	70	6139	987	017
42	3591	688	312	75	8734	1.002252	0.997748
43	4490	780	220	80	983.0647	447	559
44	5391	872	128	85	1818	566	440
				90	2213	607	400

The true acceleration due to gravity is probably about 14 mGal less than the value calculated from the international gravity formula¹².

Several new determinations of the acceleration due to gravity have recently been made¹³. The reference value of the acceleration due to gravity in the Potsdam system has meanwhile been lowered by 14 mGal following the resolutions adopted by the International Association of Geodesy¹⁴ and by the International Committee of Weights and Measures¹⁵ under the powers conferred on it by the 11th General Conference of Weights and Measures¹⁶.

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For each element the following are given: atomic number (*italics*), symbol, atomic weight (relative atomic mass)²

Period	Group I a b	Group II a b	Group III a b	Group IV a b	Group V a b	Group VI a b	Group VII a b	Group VIII a b ³
1	1. H 1.00797 ⁴							2. He 4.0026
2	3 Li 6.939	4 Be 9.0122	5 B 10.811 ⁴	6 C 12.01115 ⁴	7 N 14.0067	8 O 15.9994 ⁴	9 F 18.9984	10 Ne 20.179 ⁴
3	11 Na 22.9898	12 Mg 24.305	13 Al 26.9815	14 Si 28.086 ⁴	15 P 30.9738	16 S 32.064 ⁴	17 Cl 35.453 ⁴	18 Ar 39.948
4 (3 d)	19 K 39.102	20 Ca 40.08	21 Sc 44.956	22 Ti 47.90	23 V 50.942	24 Cr 51.996	25 Mn 54.9380	26 Fe; 27 Co; 28 Ni 55.847 ⁴ 58.9332 58.71
	29 Cu 63.546 ⁴	30 Zn 65.37	31 Ga 69.72	32 Ge 72.59	33 As 74.9216	34 Se 78.96	35 Br 79.904 ⁴	36 Kr 83.80
5 (4 d)	37 Rb 85.47	38 Sr 87.62	39 Y 88.905	40 Zr 91.22	41 Nb 92.906	42 Mo 95.94	43 Tc (99)*	44 Ru; 45 Rh; 46 Pd 101.07 102.905 106.4
	47 Ag 107.868 ⁴	48 Cd 112.40	49 In 114.82	50 Sn 118.69	51 Sb 121.75	52 Te 127.60	53 I 126.9044	54 Xe 131.30
6 (3 d) (4 f)	55 Cs 132.903	56 Ba 137.34	57 La 138.91 [4f]	58 Ce 140.12	59 Pr 140.907	60 Nd 144.24	61 Pm (147)*	62 Sm 150.35
	79 Au 196.967	80 Hg 200.59	81 Tl 204.37	82 Pb 207.19	83 Bi 208.980	84 Po (210)*	85 At (210)	86 Rn (222)
7 (6 d) (3 f)	87 Fr (223)	88 Ra (226)	89 Ac (227) [5f]					

Lanthanides (rare-earth elements)

4f	58 Ce 140.12	59 Pr 140.907	60 Nd 144.24	61 Pm (147)*	62 Sm 150.35	63 Eu 151.96	64 Gd 157.25	65 Tb 158.924	66 Dy 162.50	67 Ho 164.930	68 Er 167.26	69 Tm 168.934	70 Yb 173.04	71 Lu 174.967
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Actinides

5f	90 Th 232.038	91 Pa (231)	92 U 238.03	93 Np (237)	94 Pu (244)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (252)*	99 Es (254)	100 Fm (257)	101 Md (257)	102 No (255)	103 Lr (256)
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¹ Adapted from Eucken, A. (Ed.), *Landolt-Börnstein, Zahlenwerte und Funktionen aus Physik, Chemie, Astronomie, Graphik und Technik*, vol. 1 *Atom- und Molekularphysik*, Part 1 *Atoms and Ions*, 6th ed., Springer, Berlin, 1950, page 11.

² Based on the assigned mass 12 for the carbon isotope ¹²C and taken from the Table of Atomic Weights 1967 (International Union of Pure and Applied Chemistry, *Comptes rendus de la 24^e Conférence*, 1967, Butterworth, London, 1968, page 130 sq.). A value in parentheses is the mass number of the most stable known isotope or, when marked with an

Chemical Elements - Alphabetical Table

Name	Symbol	Atomic number	Atomic weight ¹ 1967	Name	Symbol	Atomic number	Atomic weight 1967
Actinium	Ac	89	(227)	Molybdenum...	Mo	42	95.94
Aluminium	Al	13	26.9815	Neodymium ...	Nd	60	144.24
Americium	Am	95	(243)	Neon	Ne	10	20.179 ³
Antimony	Sb	51	121.75	Neptunium	Np	93	(237)
Argon	Ar	18	39.948	Nickel	Ni	28	58.71
Arsenic	As	33	74.9216	Niobium	Nb	41	92.906
Astatine	At	85	(210)	Niton	Nt	See Radon	
Barium	Ba	56	137.34	Nitrogen	N	7	14.0067
Berkelium	Bk	97	(247)	Nobelium	No	102	(255)
Beryllium	Be	4	9.0122	Osmium	Os	76	190.2
Bismuth	Bi	83	208.980	Oxygen	O	8	15.9994 ²
Boron	B	5	10.811 ²	Palladium	Pd	46	106.4
Bromine	Br	35	79.904 ³	Phosphorus	P	15	30.9738
Cadmium	Cd	48	112.40	Platinum	Pt	78	195.09
Caesium	Cs	55	132.905	Plutonium	Pu	94	(244)
Calcium	Ca	20	40.08	Polonium	Po	84	(210)*
Californium	Cf	98	(252)*	Potassium	K	19	39.102
Carbon	C	6	12.01115 ²	Praseodymium .	Pr	59	140.907
Cassiopeium ...	Cp	See Lutetium		Promethium ...	Pm	61	(147)*
Cerium	Ce	58	140.12	Protactinium ...	Pa	91	(231)
Chlorine	Cl	17	35.453 ³	Radium	Ra	88	(226)
Chromium	Cr	24	51.996	Radon	Rn	86	(222)
Cobalt	Co	27	58.9332	Rhenium	Re	75	186.2
Columbium	Cb	See Niobium		Rhodium	Rh	45	102.905
Copper	Cu	29	63.546 ³	Rubidium	Rb	37	85.47
Curium	Cm	96	(247)	Ruthenium	Ru	44	101.07
Dysprosium	Dy	66	162.50	Samarium	Sm	62	150.35
Einsteinium	Es	99	(254)	Scandium	Sc	21	44.956
Emanation	Em	See Radon		Selenium	Se	34	78.96
Erbium	Er	68	167.26	Silicon	Si	14	28.086 ²
Europium	Eu	63	151.96	Silver	Ag	47	107.868 ³
Fermium	Fm	100	(257)	Sodium	Na	11	22.98976
Fluorine	F	9	18.9984	Strontium	Sr	38	87.62
Francium	Fr	87	(223)	Sulphur	S	16	32.064 ²
Gadolinium	Gd	64	157.25	Tantalum	Ta	73	180.948
Gallium	Ga	31	69.72	Technetium	Tc	43	(99)*
Germanium	Ge	32	72.59	Tellurium	Te	52	127.60
Glucinium	Gl	See Beryllium		Terbium	Tb	65	158.924
Gold	Au	79	196.967	Thallium	Tl	81	204.37
Hafnium	Hf	72	178.49	Thorium	Th	90	232.038
Helium	He	2	4.0026	Thulium	Tm	69	168.934
Holmium	Ho	67	164.930	Tin	Sn	50	118.69
Hydrogen	H	1	1.00797 ²	Titanium	Ti	22	47.90
Illinium	Il	See Promethium		Tungsten	W	74	183.85
Indium	In	49	114.82	Uranium	U	92	238.03
Iodine	I	53	126.9044	Vanadium	V	23	50.942
Iridium	Ir	77	192.2	Wolfram	W	See Tungsten	
Iron	Fe	26	55.847 ³	Xenon	Xe	54	131.30
Krypton	Kr	36	83.80	Ytterbium	Yb	70	173.04
Lanthanum	La	57	138.91	Yttrium	Y	39	88.905
Lawrencium ...	Lr	103	(256)	Zinc	Zn	30	65.37
Lead	Pb	82	207.19	Zirconium	Zr	40	91.22
Lithium	Li	3	6.939				
Lutetium	Lu	71	174.97				
Magnesium	Mg	12	24.305				
Manganese	Mn	25	54.9380				
Mendelevium ..	Md	101	(257)				
Mercury	Hg	80	200.59				

¹ See footnote 2, page 231.² See footnote 4, page 231.³ See footnote 5, page 231.

mbol	Name	Atomic number	Atomic weight [†] 1967	Symbol	Name	Atomic number	Atomic weight [†] 1967
Ac	Actinium	89	(227)	Mo	Molybdenum . . .	42	95.94
Ag	Silver	47	107.868 [‡]	N	Nitrogen	7	14.0067
Al	Aluminium	13	26.9815	Na	Sodium	11	22.9898
Am	Americium	95	(243)	Nb	Niobium	41	92.906
Ar	Argon	18	39.948	Nd	Neodymium . . .	60	144.24
As	Arsenic	33	74.9216	Ne	Neon	10	20.179 [‡]
At	Astatine	85	(210)	Ni	Nickel	28	58.71
Au	Gold	79	196.967	No	Nobelium	102	(255)
B	Boron	5	10.811 [‡]	Np	Neptunium . . .	93	(237)
Ba	Barium	56	137.34	Nt	Niton	See Rn	
Be	Beryllium	4	9.0122	O	Oxygen	8	15.9994 [‡]
Bi	Bismuth	83	208.980	Os	Osmium	76	190.2
Bk	Berkelium	97	(247)	P	Phosphorus . . .	15	30.9738
Br	Bromine	35	79.904 [‡]	Pa	Protactinium . .	91	(231)
C	Carbon	6	12.01115 [‡]	Pb	Lead	82	207.19
Ca	Calcium	20	40.08	Pd	Palladium	46	106.4
Cb	Columbium	See Nb		Pm	Promethium . . .	61	(147)*
Cd	Cadmium	48	112.40	Po	Polonium	84	(210)*
Ce	Cerium	58	140.12	Pr	Praseodymium . .	59	140.907
Cf	Californium	98	(252)*	Pt	Platinum	78	195.09
Cl	Chlorine	17	35.453 [‡]	Pu	Plutonium	94	(244)
Cm	Curium	96	(247)	Ra	Radium	88	(226)
Co	Cobalt	27	58.9332	Rb	Rubidium	37	85.47
Cp	Cassiopeium	See Lu		Re	Rhenium	75	186.2
Cr	Chromium	24	51.996	Rh	Rhodium	45	102.905
Cs	Cesium	55	132.905	Rn	Radon	86	(222)
Cu	Copper	29	63.546 [‡]	Ru	Ruthenium	44	101.07
Dy	Dysprosium	66	162.50	S	Sulphur	16	32.064 [‡]
Em	Emanation	See Rn		Sb	Antimony	51	121.75
Er	Erbium	68	167.26	Sc	Scandium	21	44.956
Es	Einsteinium	99	(254)	Se	Selenium	34	78.96
Eu	Europium	63	151.96	Si	Silicon	14	28.086 [‡]
F	Fluorine	9	18.9984	Sm	Samarium	62	150.35
Fe	Iron	26	55.847 [‡]	Sn	Tin	50	118.69
Fm	Fermium	100	(257)	Sr	Strontium	38	87.62
Fr	Francium	87	(223)	Ta	Tantalum	73	180.948
Ga	Gallium	31	69.72	Tb	Terbium	65	158.924
Gd	Gadolinium	64	157.25	Tc	Technetium . . .	43	(99)*
Ge	Germanium	32	72.59	Te	Tellurium	52	127.60
Gl	Glucinium	See Be		Th	Thorium	90	232.038
H	Hydrogen	1	1.00797 [‡]	Ti	Titanium	22	47.90
He	Helium	2	4.0026	Tl	Thallium	81	204.37
Hf	Hafnium	72	178.49	Tm	Thulium	69	168.934
Hg	Mercury	80	200.59	U	Uranium	92	238.03
Ho	Holmium	67	164.930	V	Vanadium	23	50.942
I	Iodine	53	126.9044	W	Tungsten	74	183.85
Il	Illium	See Pm		Xe	Xenon	54	131.30
In	Indium	49	114.82	Y	Yttrium	39	88.905
Ir	Iridium	77	192.2	Yb	Ytterbium	70	173.04
K	Potassium	19	39.102	Zn	Zinc	30	65.37
Kr	Krypton	36	83.80	Zr	Zirconium	40	91.22
La	Lanthanum	57	138.91				
Li	Lithium	3	6.939				
Lr	Lawrencium	103	(256)				
Lu	Lutetium	71	174.97				
Md	Mendelevium	101	(257)				
Mg	Magnesium	12	24.305				
Mn	Manganese	25	54.9380				

[†] See footnote 2, page 231[‡] See footnote 4, page 231^{*} See footnote 5, page 231

Atomic number		Symbol	Element English French German	Atomic weight 1967 or [mol. wt.]	Valency	Melting point ² at 760 mm Hg (unless otherwise stated) °C	Boiling point ² at 760 mm Hg (unless otherwise stated) °C	Density ² Gases: g/l at 760 mm Hg and 0 °C Others: g/cm ³ or specific gravity 20°/4 °C (unless otherwise stated)	Earth's crust, hy- drosphere, atmos- phere ³ %	Atmo- sphere (tropo- sphere) ⁴ vol %	Universe (atoms per 10 ⁸ Si atoms) ⁵	Human body ⁶ %	Isotope (mass number A)	Relative abun- dance atoms %	Mass ^a	Mode of decay ⁹	Energy in MeV and per- centage of decay	Half- life ¹⁰
1	H	[H] [H ₂]	Hydrogen ¹¹ Hydrogène Wasserstoff	1.00797 ¹² [2.01594]	1	-259.14	-252.5	gas liquid	0.88	0.00005	4.00 × 10 ¹⁰	10.0	¹ H(H) ² H(D) ³ H(T)	99.985 0.015 see ref. ¹³	1.00783 2.01410 3.016049	β- no γ	0.0181 (100%)	12.26 y
2	He	[He]	Helium Hélium Helium	4.0026	0	-272.2 at 26 atm	-268.6	gas	4.2 × 10 ⁻⁷	0.000524	3.08 × 10 ⁹		³ He ⁴ He	1.3 × 10 ⁻⁴ (in the at- mosphere) ~100	3.01603 4.00260			
3	Li	[Li]	Lithium Lithium Lithium	6.939	1	179	1317	solid liquid	0.006		100		⁶ Li ⁷ Li	7.42 92.58	6.01513 7.01601			
4	Be	[Be]	Beryllium Béryllium Beryllium	9.0122	2	1278 ± 5	2970	solid	5.3 × 10 ⁻⁴		20		⁹ Be	100	9.01219			
5	B	[B] [Bore Bor]	Boron Bore Bor	10.811 ¹²	3	2300	(sublimes 2550)	crystalline amorphous	0.0016		24	< 1.4 × 10 ⁻⁵	¹⁰ B ¹¹ B	19.6 80.4	10.01294 11.00931			
6	C	[C] [Carbone Kohlenstoff]	Carbon Carbone Kohlenstoff	12.01115 ¹²	2, 4	3550 (sublimes > 3500)	4827	amorphous graphite diamond	0.087	CO: 0-trace CO ₂ : 0.0314	3.5 × 10 ⁶	18.0	¹² C ¹³ C ¹⁴ C	98.89 1.11 see ref. ¹⁴	12.00000 13.00335 14.00324			
7	N	[N] [Azote Stickstoff]	Nitrogen Azote Stickstoff	14.0067 [28.0134]	3, 5	-209.86	-195.8	gas liquid solid	0.030		6.6 × 10 ⁶	3.0	¹⁴ N ¹⁵ N	99.63 0.37	14.00307 15.00011	β- no γ	0.1567 (100%)	5.77 × 10 ³ y
8	O	[O] [Oxygène Sauerstoff]	Oxygen Oxygène Sauerstoff	15.9994 ¹² [31.9988]	2	-218.4	-182.970	gas liquid	49.5	20.9476 (O ₂) 2-7 × 10 ⁻⁶ (O ₃)	2.15 × 10 ⁷	65.0	¹⁶ O ¹⁷ O ¹⁸ O	99.759 0.037 0.204	15.99491 16.99913 17.99916			
9	F	[F] [Fluor Fluor]	Fluorine Fluor Fluor	18.9984 [37.9968]	1	-219.62 (freezing point)	-188.14	gas liquid	0.028		1600	2 × 10 ⁻³	¹⁹ F	100	18.9984			
10	Ne	[Ne]	Neon Neon Neon	20.179 ¹⁵	0	-248.67	-245.92	gas liquid	5 × 10 ⁻⁷	0.001818	8.6 × 10 ⁶		²⁰ Ne ²¹ Ne ²² Ne	90.92 0.257 8.82	19.99244 20.99385 21.99138			
11	Na	[Na]	Sodium Sodium Natrium	22.9898	1	97.81 ± 0.03	892	solid	2.63		4.38 × 10 ⁴	1.5 × 10 ⁻¹	²³ Na	100	22.98977			
12	Mg	[Mg]	Magnesium Magnésium Magnesium	24.305	2	651	1107	solid	1.95		9.12 × 10 ⁶	5 × 10 ⁻³	²⁴ Mg ²⁵ Mg ²⁶ Mg	78.70 10.13 11.17	23.98504 24.98584 25.98259			

¹³ Al	Aluminium (Aluminum)	26 981.5	3	660.1	12467	solid	2.6989	7.57	9.48 × 10 ⁻⁴	1.4 × 10 ⁻⁴	*Al	100	4.0 × 10 ⁻²³
14 Si	Silicon Aluminium	28 086.12	4	1410	2355	solid	2.33/25*	25.80	1 × 10 ⁻⁴	2 × 10 ⁻⁴	**Si	92.21 4.70 3.09	27 976.93 28 976.49 29 973.76
15 P	Phosphorus Silicium	30 973.8	3, 5	yellow 44.1	280	yellow solid red solid black solid	1.82 2.25-2.69	0.09	1 × 10 ⁻⁴	1.0	**P	100	30.97376
16 S	Sulphur (Sulfur) Sulfur Schwefel	32 064.12	2, 4, 6	rhombic 112.8 monoclinic 119.0	444 600	rhombic monoclinic solid	1.07 1.957	0.048	0-0.0001 (SO ₄)	3.75 × 10 ⁻⁴	**S	95.0 0.76 4.22 0.014	31.97207 32.97146 33.96786 35.96709
17 Cl	Chlorine [Chl] Chlor	35.45312 [70 906]	1, 2, 5, 7	-100.98 (freezing point)	-34.6	gas liquid	3.214 1.56/-33.6*	0.19	8850	1.5 × 10 ⁻⁴	**Cl	75.53 24.47	34.96885 36.96590
18 Ar	Argon Argon Argon	39 948	0	-189.2 (freezing point)	-185.7	gas liquid solid	1.7837 1.402/-185.7* 1.65/-223*	3.6 × 10 ⁻⁴	0.934	1.5 × 10 ⁻⁴	**Ar	0.337 0.063 99.60	35.96755 37.96272 39.96238
19 K	Potassium Potassium Kalium	39 102	1	63.65	754	solid	0.862	2.41	3160	2 × 10 ⁻¹	**K	93.10 0.0118	38.96371 39.96401
20 Ca	Calcium Calcium Calcium	40 08	2	842-848	1487	solid	1.55	3.38	4.90 × 10 ⁻⁴	1.5	**Ca	6.88 96.97 0.64 0.145 2.06 0.0033	40.96184 39.96259 41.05863 42.05878 43.05549 45.95369
21 Sc	Scandium Scandium Scandium	44.956	3	1539	2727	solid	2.992	5.1 × 10 ⁻⁴	28		**Sc	100	44.95592
22 Ti	Titanium Titanium Titan	47 90	2, 3, 4	1675	3260	solid	4.54	0.41	2440	<2 × 10 ⁻⁴	**Ti	7.93 7.28 73.94 5.51 5.34	45.95263 46.95176 47.94795 48.94787 49.94479
23 V	Vanadium Vanadium Vanadium (Vanadin)	50 942	2, 3, 4, 5	1890 ± 10	~3000	solid	6.11/18.7*	0.014	220	3 × 10 ⁻⁴	**V	0.24 99.76	49.94716 50.94398

1.32(0%), 1.3 × 10⁻⁴ γ
1.46
(11%)
1.51
(11%)

> 2 × 10⁻⁴ γ

β-

0.12

β-, K
γ

0.71
1.59

≈ 6 × 10⁻⁴ γ

Element English French German Latin	Atomic weight 1967 ¹	Valency	Melting point ² at 760 mm Hg (unless otherwise stated) °C	Boiling point ² at 760 mm Hg (unless otherwise stated) °C	Density ² Gases: g/l at 760 mm Hg and 0 °C Others: g/cm ³ or specific gravity 20°/4 °C (unless otherwise stated)	Natural abundance				Natural isotopes ⁷						
						Earth's crust, hydrosphere, atmosphere ³ %	Atmosphere (troposphere) ⁴ vol %	Universe (atoms per 10 ⁸ Si atoms) ⁵	Human body ⁶ %	Isotope (mass number A)	Relative abundance atoms %	Mass ⁸	Mode of decay ⁹	Energy in MeV and percentage of decay	Half-life ¹⁰	
Chromium Chrom Chrom	51.996	2, 3, 6	1890	2482	solid 7.18-7.20	0.019		7800	<9 × 10 ⁻⁶	⁵⁰ Cr ⁵² Cr ⁵³ Cr ⁵⁴ Cr ⁵⁵ Mn	4.31 83.76 9.55 2.38 100	49.94605 51.94051 52.94065 53.93888 54.93805				
Manganese Manganèse Mangan	54.9380	1, 2, 3, 4, 6, 7	1244 ± 3	2097	solid 7.21-7.44	0.085		6850	3 × 10 ⁻⁵							
Iron Fer Eisen Ferrum	55.847 ¹⁵	2, 3, 4, 6	1535	3000	solid 7.874	4.7		6.00 × 10 ⁵	6 × 10 ⁻³	⁵⁴ Fe ⁵⁶ Fe ⁵⁷ Fe ⁵⁸ Fe	5.82 91.66 2.19 0.33	53.93962 55.93493 56.93539 57.93327				
Cobalt Cobalt Cobalt	58.9332	2, 3	1492	2900	solid 8.9	0.0037		1800	<4 × 10 ⁻⁶	⁵⁹ Co	100	58.93319				
Nickel Nickel Nickel	58.71	0, 1, 2, 3	1453	2732	solid 8.902/25°	0.015		2.74 × 10 ⁴	<1.4 × 10 ⁻⁵	⁵⁸ Ni ⁶⁰ Ni ⁶¹ Ni ⁶² Ni ⁶⁴ Ni	67.88 26.23 1.19 3.66 1.08	57.93534 59.93078 60.93105 61.92835 63.92796				
Copper Cuivre Kupfer Cuprum	63.546 ¹⁵	1, 2	1083	2595	solid 8.96	0.010		212	1.4 × 10 ⁻⁴	⁶³ Cu ⁶⁵ Cu	69.09 30.91	62.92959 64.92779				
Zinc Zinc Zink	65.37	2	419.505	907	solid 7.133/25°	0.012		486	3.3 × 10 ⁻³	⁶⁴ Zn ⁶⁶ Zn ⁶⁷ Zn ⁶⁸ Zn ⁷⁰ Zn	48.89 27.81 4.11 18.57 0.62	63.92915 65.92605 66.92715 67.92487 69.92535				
Gallium Gallium Gallium	69.72	2, 3	29.78	2403	solid 5.907	0.0014		11.4		⁶⁹ Ga ⁷¹ Ga	60.4 39.6	68.92568 70.92484				
Germanium Germanium Germanium	72.59	2, 4	937.4	2830	solid 5.323/25°	5.6 × 10 ⁻⁴		50.5		⁷⁰ Ge ⁷² Ge ⁷³ Ge ⁷⁴ Ge ⁷⁶ Ge ⁷⁵ As	20.52 27.43 7.76 36.54 7.76 100	69.92428 71.92174 72.92336 73.92115 75.92136 74.92158				
Arsenic Arsenic Arsen	74.9216	3, 5	crystalline 817 at 28 atm.	crystalline 573 amorphous 473 yellow; solid 1.97		5.5 × 10 ⁻⁴		4.0	2 × 10 ⁻⁵							

Element English French German Latin	Atomic weight 1967 ¹	Valency	Melting point ² at 760 mm Hg (unless otherwise stated) °C	Boiling point ² at 760 mm Hg (unless otherwise stated) °C	Density ² Gases: g/l at 760 mm Hg and 0 °C Others: g/cm ³ or specific gravity 20°/4 °C (unless otherwise stated)	Natural abundance				Natural isotope ⁷										
						Earth's crust, hy- drosphere, atmo- sphere ³ %	Atmo- sphere (tropo- sphere) ⁴ vol %	Universe (atoms per 10 ⁸ Si atoms) ⁵	Human body ⁶ %	Isotope (mass number <i>A</i>)	Relative abun- dant atoms %	Mass ⁸	Mode of decay ²	Energy in MeV and per- centage of decay	Half- life ⁹					
Ruthenium Ruthénium Ruthenium	101.07	0, 1, 2, 3, 4, 5, 6, 7, 8	2250	(3900)	solid 12.41	2 × 10 ⁻⁶		1.49					⁹⁸ Ru ⁹⁹ Ru ⁹⁹ Ru ¹⁰⁰ Ru ¹⁰¹ Ru ¹⁰² Ru ¹⁰⁴ Ru	5.51 1.87 12.72 12.62 17.07 31.61 18.58	95.9076 97.9055 98.90608 99.90302 100.90412 101.90372 103.90553					
Rhodium Rhodium Rhodium	102.905	2, 3, 4, 5	1960	(3727 ± 100)	solid 12.41	1 × 10 ⁻⁷		0.214					¹⁰³ Rh	100	102.9048					
Palladium Palladium Palladium	106.4	2, 3, 4	1552	(2927)	solid 12.02	1 × 10 ⁻⁶		0.675					¹⁰² Pd ¹⁰⁴ Pd ¹⁰⁵ Pd ¹⁰⁶ Pd ¹⁰⁸ Pd ¹¹⁰ Pd	0.96 10.97 22.23 27.33 26.71 11.81	101.90494 103.90356 104.90464 105.9032 107.90392 109.9045					
Silver Argent Silber <i>Argentum</i>	107.868 ¹⁵	1, 2	960.8	2112	solid 10.50	1 × 10 ⁻⁵		0.26	< 1 × 10 ⁻⁶				¹⁰⁷ Ag ¹⁰⁹ Ag	51.82 48.18	106.90497 108.9047					
Cadmium Cadmium Cadmium	112.40	2	321.03	765	solid 8.65	3 × 10 ⁻⁵		0.89	4.3 × 10 ⁻⁵				¹⁰⁶ Cd ¹⁰⁸ Cd ¹¹⁰ Cd ¹¹¹ Cd ¹¹² Cd ¹¹³ Cd ¹¹⁴ Cd ¹¹⁶ Cd	1.22 0.88 12.39 12.75 24.07 12.26 28.86 7.58	105.90595 107.904 109.90297 110.90415 111.90284 112.90461 113.90357 115.90501					
Indium Indium Indium	114.82	1, 2, 3	156.61	2000 ± 10	solid 7.31	1 × 10 ⁻⁶		0.11					¹¹³ In ¹¹⁵ In	4.28 95.72	112.90428 114.90407	β ⁻	0.6 (100%)	6 × 10 ¹⁴ y		
Tin Etain Zinn <i>Stannum</i>	118.69	2, 4	231.91	2270	cubic (α) solid 5.750 tetragonal (β) solid 7.31	0.0035		1.33	4.3 × 10 ⁻⁵				¹¹² Sn ¹¹⁴ Sn ¹¹⁵ Sn ¹¹⁶ Sn ¹¹⁷ Sn ¹¹⁸ Sn ¹¹⁹ Sn ¹²⁰ Sn ¹²² Sn ¹²⁴ Sn	0.96 0.66 0.35 14.30 7.61 24.03 8.58 32.85 4.92 5.94	111.90494 113.90296 114.90353 115.90211 116.90306 117.90179 118.90339 119.90213 121.90341 123.90524					

51 Sb	Antimony Antimoine Antimon Stibium	121.75	3, 5, 630.5	1380	solid	6.691	6.5×10^{-8}	0.246	$< 1.3 \times 10^{-1}$	^{121}Sb ^{123}Sb	57.25 42.75	120.90375 122.90415
52 Te	Tellurium Tellure Tellur	127.60	2, 4, 449.5 6 ± 0.3	989.8 ± 3.8	rhombic	6.24	1×10^{-8}	4.67		^{126}Te ^{128}Te ^{129}Te ^{130}Te ^{132}Te ^{134}Te ^{136}Te	0.089 2.46 0.87 122.90418 4.61 6.99 18.71 125.90324 31.79 127.90471 32.48 129.9067 100 126.90435	119.90451 121.9030 122.90418 123.90276 124.90442 125.90324 127.90471 129.9067 126.90435
53 I	Iodine Iode Jod	126.9044	1, 3, 113.5 5, 7	184.35	gas solid	11.27 4.95	6×10^{-8}	0.1×10^{-8} 0.80 (I_2)	4×10^{-8}	^{127}I	100	126.90435
54 Xe	Xenon Xénon Xenon	131.30	0, 2, -111.9 4, 6, ± 3	-107.1 ± 3	gas liquid	5.887 ± 0.009 $3.521 - 10^9$	2.4×10^{-8}	8.7×10^{-8} 4.0		^{134}Xe ^{136}Xe ^{138}Xe ^{139}Xe ^{140}Xe ^{141}Xe ^{142}Xe ^{144}Xe ^{146}Xe ^{148}Xe ^{150}Xe	0.096 0.090 1.92 127.90354 26.44 128.90478 4.08 129.90351 21.18 130.90509 26.89 131.90416 10.44 133.9054 8.87 135.90722 100 132.90509	123.90612 125.90417 127.90354 128.90478 129.90351 130.90509 131.90416 133.9054 135.90722 132.90509
55 Cs	Cesium (Cesium) Césium Cesium	132.905	1, 28.5	690	solid	1.873	6.5×10^{-8}	10.456	$< 1.4 \times 10^{-8}$	^{133}Cs	100	132.90509
56 Ba	Barium Baryum Barium	137.34	2, 725	1140	solid	3.5	0.026	3.66	2.3×10^{-8}	^{134}Ba ^{135}Ba ^{136}Ba ^{137}Ba ^{138}Ba ^{139}Ba ^{140}Ba ^{142}Ba ^{144}Ba	0.101 0.097 131.90512 2.42 133.90431 6.59 134.9057 7.81 135.90436 11.32 136.90556 71.66 137.90501 0.089 137.90681 β^-	129.90625 131.90512 133.90431 134.9057 135.90436 136.90556 137.90501 137.90681 β^-
57 La	Lanthanum Lanthane Lanthan	138.91	3, 920	3469	solid	$5.98 - 6.186$	0.0017	2.00		^{138}La	0.205 (30%) 0.54 (15%) 0.81 (30%) 1.43 (70%) (70%)	$1.1 \times 10^{11} \text{y}$
58 Ce	Cerium Cérium Cer	140.12	3, 4, 795	3468	cubic hexagonal	α 8.23 β 6.66	0.0043	2.26		^{138}La ^{140}Ce ^{142}Ce ^{144}Ce	99.911 0.193 0.250 88.48 11.07	138.90606 135.9071 137.90572 139.90528 141.90904 α

Symbol	Element English French German	Atomic weight 1967 ¹	Valency	Melting point ² at 760 mm Hg (unless otherwise stated) °C	Boiling point ² at 760 mm Hg (unless otherwise stated) °C	Density ² Gases: g/l at 760 mm Hg and 0 °C Others: g/cm ³ or specific gravity 20 °/4 °C (unless otherwise stated)	Natural abundance				Natural isotopes ⁷							
							Earth's crust, hy- drophere, atmo- sphere ³ %	Atmo- sphere (tropo- sphere) ⁴ vol %	Universe (atoms per 10 ⁶ Si atoms) ⁵	Human body ⁶ %	Isotope (mass number A)	Relative abun- dance atoms %	Mass ⁸	Mode of decay ⁹	Energy in MeV and per- centage of decay	Half- life ¹⁰		
59 Pr	Praseo- dymium Praseodyme Praseodym	140.907	3, 4	935	3127	hexagonal cubic α 6.782 β 6.64	5.2 × 10 ⁻⁴		0.40		¹⁴¹ Pr	100	140.90739					
60 Nd	Neodymium Néodyme Neodym	144.24	3	1024	3027	hexagonal cubic α 7.004 β 6.80	0.0022		1.44		¹⁴² Nd ¹⁴³ Nd ¹⁴⁴ Nd ¹⁴⁵ Nd ¹⁴⁶ Nd ¹⁴⁸ Nd ¹⁵⁰ Nd	27.11 12.17 23.85 8.30 17.22 5.73 5.62	141.90748 142.90962 143.9099 144.91216 145.91269 147.91648 149.92071	α	1.8	≈ 5 × 10 ¹⁵ y		
61 Pm	Promethium Prométhium Promethium	(147)*	3	1035	2730						¹⁴⁷ Pm	see ref. 16	146.91486	β ⁻	0.225 (100%) 0.10 (10 ⁻² %)	2.5 y		
62 Sm	Samarium Samarium Samarium	150.35	2, 3	1072	1900	rhombohedral α 7.536 β 7.40	6 × 10 ⁻⁴		0.664		¹⁴⁴ Sm ¹⁴⁷ Sm ¹⁴⁸ Sm ¹⁴⁹ Sm ¹⁵⁰ Sm ¹⁵² Sm ¹⁵⁴ Sm	3.09 14.97 11.24 13.83 7.44 26.72 22.71	143.91165 146.91462 147.91456 148.91693 149.91701 151.91949 153.92201	α α α α	2.24 2.14 1.84	1.06 × 10 ¹¹ y 1.2 × 10 ¹³ y ~ 4 × 10 ¹⁴ y		
63 Eu	Europium Europium Europium	151.96	2, 3	826	1439	solid	9.9 × 10 ⁻⁵		0.187		¹⁵¹ Eu ¹⁵³ Eu	47.82 52.18	150.91963 152.92086					
64 Gd	Gadolinium Gadolinium Gadolinium	157.25	3	1312	~3000	hexagonal cubic α 7.895 β 7.80	5.9 × 10 ⁻⁴		0.684		¹⁵² Gd ¹⁵⁴ Gd ¹⁵⁵ Gd ¹⁵⁶ Gd ¹⁵⁷ Gd ¹⁵⁸ Gd ¹⁶⁰ Gd	0.20 2.15 14.73 20.47 15.68 24.87 21.90	151.91953 153.92072 154.92259 155.9221 156.92394 157.9241 159.92712	α	2.15	1.1 × 10 ¹⁴ y		
65 Tb	Terbium Terbium Terbium	158.924	3, 4	1356	2800	solid	8.5 × 10 ⁻⁵		0.0956		¹⁵⁹ Tb	100	158.92495					
66 Dy	Dysprosium Dysprosium Dysprosium	162.50	3	1407	2600	solid	4.2 × 10 ⁻⁴		0.556		¹⁵⁶ Dy ¹⁵⁸ Dy ¹⁶⁰ Dy ¹⁶¹ Dy ¹⁶² Dy ¹⁶³ Dy	0.052 0.090 2.29 18.88 25.53 24.97	155.92376 157.92396 159.92483 160.9266 161.92647 162.92837					

Atomic number Z	Symbol	Element English French German Latin	Atomic weight 1967 ¹	Valency	Melting point ² at 760 mm Hg (unless otherwise stated) °C	Boiling point ² at 760 mm Hg (unless otherwise stated) °C	Density ² Gases: g/l at 760 mm Hg and 0 °C Others: g/cm ³ or specific gravity 20°/4 °C (unless otherwise stated)	Natural abundance				Natural isotopes ⁷								
								Earth's crust, hydrosphere, atmosphere ³ %	Atmosphere (troposphere) ⁴ vol %	Universe (atoms per 10 ⁸ Si atoms) ⁵ %	Human body ⁶ %	Isotope (mass number A)	Relative abundance atoms %	Mass ⁸	Mode of decay ⁹	Energy in MeV and percentage of decay	Half-life ¹⁰			
76	Os	Osmium Osmium Osmium	190.2	2, 3, 4, 8	3000 ± 10	(5000)	solid 22.57 (heaviest element)	1 × 10 ⁻⁶	1.00			¹⁸⁴ Os ¹⁸⁶ Os ¹⁸⁷ Os ¹⁸⁸ Os ¹⁸⁹ Os ¹⁹⁰ Os ¹⁹² Os	0.018 1.59 1.64 13.3 16.1 26.4 41.0	183.95256 185.95394 186.95596 187.95597 188.95825 189.9586 191.96141						
77	Ir	Iridium Iridium Iridium	192.2	3, 4	2443	(4527 ± 100)	solid 22.42/17°	1 × 10 ⁻⁷	0.821			¹⁹¹ Ir ¹⁹³ Ir	37.3 62.7	190.96085 192.96328						
78	Pt	Platinum Platine Platin	195.09	1, 2, 3, 4	1769	(3827 ± 100)	solid 21.45	5 × 10 ⁻⁷	1.625			¹⁹⁰ Pt ¹⁹² Pt ¹⁹⁴ Pt ¹⁹⁵ Pt ¹⁹⁶ Pt ¹⁹⁸ Pt	0.0127 0.78 32.9 33.8 25.3 7.21	189.95995 191.96143 193.96281 194.96482 195.96498 197.96753	α α	3.11 ~2.6	7 × 10 ¹¹ y ~10 ¹⁵ y			
79	Au	Gold Or Gold Aurum	196.967	1, 3	1063.0	2966	solid 19.32	5 × 10 ⁻⁷	0.145	< 1 × 10 ⁻⁶		¹⁹⁷ Au	100	196.96655						
80	Hg	Mercury Mercure Quecksilber Hydrargyrum	200.59	1, 2	-38.87	356.58	14.43/-38.87° 13.595/0° 13.546/20° 17	4 × 10 ⁻⁵	0.284			¹⁹⁶ Hg ¹⁹⁸ Hg ¹⁹⁹ Hg ²⁰⁰ Hg ²⁰¹ Hg ²⁰² Hg ²⁰⁴ Hg	0.146 10.02 16.84 23.13 13.22 29.80 6.85	195.96582 197.96677 198.96826 199.96834 200.97032 201.97063 203.97348						
81	Tl	Thallium Thallium Thallium	204.37	1, 3	303.5	1457 ± 10	solid 11.85	3 × 10 ⁻⁵	0.108			²⁰³ Tl ²⁰⁵ Tl ²⁰⁶ Tl (Radium E) ²⁰⁷ Tl (Actinium C') ²⁰⁸ Tl (Thorium C')	29.50 70.50	202.97233 204.97446 205.97608 206.97745 207.98201	β- no γ β- γ β- γ	1.51 1.44 0.89 1.80 1.52 1.28 2.615 0.511 0.860 0.000	4.20 min 4.78 min 3.1 min			

Z	Atomic number	Symbol	Element English French German	Atomic weight 1967 ¹	Valency	Melting point ² at 760 mm Hg (unless otherwise stated) °C	Boiling point ² at 760 mm Hg (unless otherwise stated) °C	Density ² Gases: g/l at 760 mm Hg and 0 °C Others: g/cm ³ or specific gravity 20 °/4 °C (unless otherwise stated)	Natural abundance			Natural isotopes ⁷							
									Earth's crust, hy- drosphere, atmo- sphere ³ %	Atmo- sphere (tropo- sphere) ⁴ vol %	Universe (atoms per 10 ⁸ Si atoms) ⁵	Human body ⁶ %	Isotope (mass number A)	Relative abun- dance atoms %	Mass ⁸	Mode of decay ⁹	Energy in MeV and percentage of decay	Half- life ¹⁰	
90	Th		Thorium (continued)									²³⁰ Th (Ionium)		230.03308	α	4.682 4.615 4.240-4.474	(76%) (24%)	8×10^4 y	
															γ	0.0677 0.110 0.144 0.19 0.203 0.235 0.255 0.30 0.084 0.017-0.31	(0.59%) (1×10^{-4} %) (0.77%) (1.4×10^{-2} %) ($\approx 5 \times 10^{-4}$ %) ($\approx 5 \times 10^{-4}$ %) (1.7×10^{-4} %) (78%) (11%) (13%)	25.6 h	
												²³¹ Th (Uranium Y)		231.03635	β^- γ (>10)				
												²³² Th		232.03821	α	4.007 3.99 0.059 0.192 0.10 0.092 0.063 0.029	(76%) (24%) (24%) (65%) (35%)	1.39×10^{10} y	
												²³³ Th (Uranium X ₁)		234.04357	γ β^-				24.10 d
91	Pa		Protactinium Protactinium Protactinium	(231)	4, 5 ~1230?			solid 15.37	9×10^{-11}			²³¹ Pa		231.03594	α	5.001 5.017 5.046 4.938 4.666-4.971 0.29 0.027-0.356 0.58 2.31 0.043 0.23-1.83	(24%) (23%) (10%) (22%)	3.43×10^4 y	
												²³⁴ Pa (Uranium X ₂)			γ (>10) β^- γ (>10) IT		(99%) (1%)	1.18 min	
												²³⁵ Pa (Uranium Z)		234.04337	β^- γ (>10)				6.66 h
																0.23-1.35 0.044 0.100 0.228 0.000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000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92 U	Uranium	238.03	3.4, 11.2 ± 5.6 ± 0.8	381.0	Barium	(Uranium II)	99.27	238.05076 ±	Y	7.11 ± 0.063	7.13 × 10 ⁻⁷ y
	Uranium					99.27				0.118	(6.7%)
	Uran									4.559	(25%)
										4.370	(25%)
										4.354	(14%)
										4.333	(8%)
										4.318	(5.8%)
										4.117	
										0.074	(9%)
										0.094	(5%)
										0.1096	(12%)
										0.144	(12%)
										0.165	(5.5%)
										0.185	(5.5%)
										0.203	(5.5%)
										0.2890	(77%)
										0.367	(23%)
										0.385	(23%)
										4.195	
										4.14	
										0.048	

¹ See footnote 2, page 231

² From HAYES, C. R., in WEAST et al. (Eds.), *Handbook of Chemistry and Physics*, 59th ed., The Chemical Rubber Co., Cleveland, 1958, page B-97. HAYES, C. A. (Ed.), *Revised Ninth Handbook*, 2nd ed., Reinhold, London, 1961.

³ Values are total percentages in the lithosphere (outer 10 miles), hydrosphere and atmosphere (from RAZ, H., *Lehrbuch der anorganischen Chemie*, 11th ed., vol. 2, Akademische Verlagsgesellschaft, Leipzig, 1951, page 769).

⁴ Dry atmosphere at sea level. From *Manual of the IC-60 Handbook of Atomic Weights*, International Union of Pure and Applied Chemistry, 1964.

⁵ From SCHNEIDER, H. A., *J. Chem. Phys.*, 18, 217 (1950), for As from SCHNEIDER and BALASH, *J. Chem. Phys.*, 19, 83 (1956), for Zr from

SCHNEIDER and BALASH, *J. Chem. Phys.*, 19, 573 (1956), for Nb from SCHNEIDER and BALASH, *J. Chem. Phys.*, 18, 229 (1955). See also "Composition of the Body", pages 517-522.

⁷ From HAYES, C. R., in WEAST et al. (Eds.), *Handbook of Chemistry and Physics*, 59th ed., The Chemical Rubber Co., Cleveland, 1958, page B-4.

⁸ Unified scale of atomic masses (1963 scale, see page 226). Values from KOSIG et al., *Nucl. Phys.*, 31, 19 (1962).

⁹ α = alpha particle (helium nucleus = 2 protons + 2 neutrons), β^- = beta particle (electron), γ = gamma ray, K = orbital electron capture.

¹⁰ t_1 = age of the body, t_2 = age of the sample, t_3 = age of the sample, t_4 = age of the sample, t_5 = age of the sample, t_6 = age of the sample, t_7 = age of the sample, t_8 = age of the sample, t_9 = age of the sample, t_{10} = age of the sample.

¹¹ Normal molecular hydrogen is a mixture of ortho- and para hydrogen (molecules in which the two nuclei have respectively parallel and antiparallel spins) in the proportions 3:1.

¹² See footnote 6, page 231

¹³ A disintegration product of ²³⁸U in the atmosphere due to the action of cosmic rays. The ratio of ¹⁴C to ¹²C in atmospheric hydrogen is of the order of 10⁻¹². Cf. GROSS et al., *Phys. Rev.*, 91, 250 (1954).

¹⁴ A disintegration product of ²³⁸U in the atmosphere due to the action of naturally occurring neutrons.

¹⁵ See footnote 6, page 231

¹⁶ A disintegration product of ²³⁸U due to the action of naturally occurring neutrons.

¹⁷ For density of mercury under standard conditions see page 230. For internationally accepted density values for mercury at different temperatures see LINDSEY, R. B., in GAFF, D. E. (Ed.), *American Institute of Physics Handbook*, McGraw-Hill, New York, 1957, pages 2-140.

Atomic number Z	Symbol	Transuranic element ¹	Atomic weight 1967 ²	Valency ³	Melting point ³ °C	Boiling point ³ °C	Density ³ g/cm ³	Isotopes				
								Isotope (mass number A)	Mass ⁵	Mode of decay ⁶ (radiation)	Energy in MeV ⁴ (percentage of decay in brackets)	Half-life ⁷
93	Np	Neptunium	(237)	3, 4, 5, 6	640±1		solid	²³⁷ Np	237.04803	α	4.787 (53%) 4.767 (29%) 4.52-4.87 0.020 0.087 (14%) 0.0296 (14%) 0.0568 (0.8%) 0.143 (0.1%) 0.175 (0.3%) 0.200	2.14×10 ⁶ y
94	Pu	Plutonium	(244)	3, 4, 5, 6	639.5±2	3235±19	solid	²⁴⁴ Pu		α		8.2×10 ⁷ y
95	Am	Americium	(243)	3, 4, 5, 6	>850		solid	²⁴³ Am	243.06138	α, γ		7950 y
96	Cm	Curium	(247)	3			solid	²⁴⁷ Cm		α		1.6×10 ⁷ y
97	Bk	Berkelium	(247)	3, 4				²⁴⁷ Bk	247.07018	α, γ		1.4×10 ³ y
98	Cf	Californium	(252)*	3				²⁵² Cf		α		2.65 y
99	Es	Einsteinium	(254)	3				²⁵⁴ Es	254.08811	α, γ		270 d
100	Fm	Fermium	(257)	3				²⁵⁷ Fm		α		80 d
101	Md	Mendelevium	(257)	3				²⁵⁷ Md		α, K		3.0 h
102	No	Nobelium	(255)					²⁵⁵ No		α		3.0 min
103	Lr	Lawrencium	(256)					²⁵⁶ Lr		α		45 s

¹ The transuranic elements have become known as artificially produced elements. However, since they have in the past occurred naturally (or are still, like ²³⁸U, identifiable in very small amounts in nature) they can be regarded also as naturally occurring elements. In a sense they are elements which as a result of their short half-lives have become extinct.

² See footnote 2, page 231.

³ From HAMMOND, C. R., in WYSE et al. (Eds.), *Handbook of Chemistry*

and Physics, 49th ed., The Chemical Rubber Co., Cleveland, 1968, page B-97; HAMPER, C. A. (Eds.), *Rare Metals Handbook*, 2nd ed., Reinhold, London, 1961.

⁴ Values from HILARY, R. L., in WYSE et al. (Eds.), *Handbook of Chemistry and Physics*, 49th ed., The Chemical Rubber Co., Cleveland, 1968, page D-4.

⁵ Unified scale of atomic masses (12C scale; see page 226). Values from KONTO et al., *Nucl. Phys.*, 31, 18 (1962).

⁶ α = alpha particle (helium nucleus = 2 protons + 2 neutrons), γ = gamma ray, K = orbital electron capture from K shell.

⁷ y = year, d = day, h = hour, min = minute, s = second. Values from International Union of Pure and Applied Chemistry, *Comptes rendus de la 24^e Conférence*, 1967, Butterworth, London, 1968, page 140.

Electronic Configurations of the Elements¹

249

 Z = atomic number, E_r = resonance energy (eV), E_i = ionization energy (eV), E_{r1} = resonance energy of singly-ionized atom (eV)

Z	Element	E_r	E_i	E_{r1}	K 1s	L 2s 2p	M 3s 3p 3d	N 4s 4p 4d 4f	O 5s 5p 5d 5f	P 6s 6p 6d	Q 7s
1	H	10.19	13.60		1						
2	He	21.20	24.58		2						
3	Li	1.35	5.39	40.8	2	1					
4	Be	5.28	9.32	5.96	2	2					
5	B	4.96	8.33	9.10	2	2	1				
6	C	7.48	11.26	9.29	2	2	2				
7	N	10.3	14.44	11.4	2	2	2	1			
8	O	9.32	13.61	14.8	2	2	2	2			
9	F	12.98	17.42	20.42	2	2	2	2	1		
10	Ne	15.84	21.56	26.89	2	2	2	2	2		
11	Na	2.10	5.14	33.5	2	2	2				
12	Mg	4.34	7.64	4.42	2	2	2				
13	Al	3.14	5.98	7.42	2	2	2	1			
14	Si	4.92	8.15	6.86	2	2	2	2			
15	P	6.94	10.95	8.09	2	2	2	2			
16	S	6.86	10.36	9.84	2	2	2	2			
17	Cl	9.21	13.01	11.56	2	2	2	2			
18	Ar	11.53	15.75	13.47	2	2	2	2			
19	K	1.61	4.34	20.6	2	2	2				
20	Ca	2.95	6.11	3.12	2	2	2				
21	Sc	2.32	6.56	3.40	2	2	2	1			
22	Ti	1.97	6.83	3.66	2	2	2	2			
23	V	2.24	6.74	4.40	2	2	2	2			
24	Cr	2.89	6.76	6.00	2	2	2	2			
25	Mn	3.07	7.45	4.76	2	2	2	2			
26	Fe	3.21	7.90	5.29	2	2	2	2			
27	Co	5.37	7.86	5.83	2	2	2	2			
28	Ni	5.14	7.63	6.39	2	2	2	2			
29	Cu	3.79	7.72	8.26	2	2	2	2			
30	Zn	4.03	9.39	5.91	2	2	2	2			
31	Ga	5.07	6.00	8.78	2	2	2	2			
32	Ge	4.64	8.13	10.06	2	2	2	2			
33	As	6.28	9.81	9.14	2	2	2	2			
34	Se	6.52	9.75	10.39	2	2	2	2			
35	Br	8.32	11.84	12.21	2	2	2	2			
36	Kr	10.03	15.99	15.82	2	2	2	2			
37	Rb	4.17	17.8		2	2	2				
38	Sr	2.49	5.49	2.94	2	2	2				
39	Y	1.99	4.57	2.91	2	2	2				
40	Zr	2.02	6.95	3.47	2	2	2				
41	Nb	2.97	6.77	4.13	2	2	2				
42	Mo	3.18	7.18	6.08	2	2	2				
43	Tc	2.88	7.43	6.68	2	2	2				
44	Ru	3.26	7.5	6.29	2	2	2				
45	Rh	3.55	7.7	4.97	2	2	2				
46	Pd	4.22	8.33	11.12	2	2	2				
47	Ag	3.26	5.58	11.1	2	2	2				
48	Cd	3.80	8.99	7.47	2	2	2				
49	In	3.02	5.78	7.82	2	2	2				
50	Sn	4.30	7.33	7.30	2	2	2				
51	Pb	3.56	8.64	9.56	2	2	2				
52	Bi	3.78	8.03	9.12	2	2	2				
53	Po	7.67	10.44	10.04	2	2	2				
54	Xe	8.44	12.13	11.27	2	2	2				
55	Cs	1.38	3.89	15.2	2	2	2				
56	Ba	2.24	5.21	2.51	2	2	2				
57	La	1.64	3.41	1.75	2	2	2				
58	Ce		6.91	2.72	2	2	2				
59	Pr		5.76	2.81	2	2	2				
60	Nd		6.31	2.63	2	2	2				
61	Pm				2	2	2				
62	Sm	1.71	5.6	2.63	2	2	2				
63	Eu	1.74	5.67	2.35	2	2	2				
64	Gd	1.63	6.16	3.18	2	2	2				
65	Tb		6.74		2	2	2				
66	Dy		6.82		2	2	2				
67	Ho				2	2	2				
68	Er	2.627		2.68	2	2	2				
69	Tm		6.2	3.55	2	2	2				
70	Yb	2.23	5.0	3.58	2	2	2				
71	Lu	2.167	5.5	3.43	2	2	2				
72	Hf	2.19	5.5	3.63	2	2	2				
73	Ta	2.49	7.98	4.48	2	2	2				
74	W				2	2	2				
75	Re	3.57	7.88		2	2	2				
76	Os	2.80	6.7		2	2	2				
77	Ir	4.65	9.2	4.38	2	2	2				
78	Pt	4.04	6.97	7.61	2	2	2				
79	Au	4.63	9.22		2	2	2				
80	Hg	4.89	10.43	6.38	2	2	2				
81	Tl	5.28	6.11	9.36	2	2	2				
82	Pb	4.44	6.43	7.35	2	2	2				
83	Bi	4.04	8.0	6.63	2	2	2				
84	Po		7.25		2	2	2				
85	At				2	2	2				
86	Rn	6.78	10.75		2	2	2				
87	Fr	2.57	5.28	2.65	2	2	2				
88	Ra				2	2	2				
89	Ac				2	2	2				
90	Th			2.12	2	2	2				
91	Pa				2	2	2				
92	U	1.44	~ 4	3.21	2	2	2				
93	Np				2	2	2				
94	Pu				2	2	2				
95	Am				2	2	2				
96	Cm				2	2	2				
97	Bk				2	2	2				
98	Cf				2	2	2				
99	Es				2	2	2				
100	Fm				2	2	2				
101	Md				2	2	2				

¹ From MURPHY and BORTON, *L'analyse spectrale quantitative par la Raoult*, Masson, Paris, 1954. Reproduced by permission of the authors and publishers.Data for elements 94-101 from WEAST et al. (Eds.), *Handbook of Chemistry and Physics*, 49th ed., The Chemical Rubber Co., Cleveland, 1968, page B.2.

Multiples of Atomic Weights of Important Elements

This table is based on the Table of Atomic Weights 1967 (see footnote 2, page 231)

Z	Sym- bol		0	1	2	3	4	5	6	7	8	9	
1	H	Hydrogen	0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190	0.000 00 10.079 70 20.159 40 30.239 10 40.318 80 50.398 50 60.478 20 70.557 90 80.637 60 90.717 30 100.797 00 110.876 70 120.956 40 131.036 10 141.115 80 151.195 50 161.275 20 171.354 90 181.434 60 191.514 30	1.007 97 11.087 67 21.167 37 31.247 07 41.326 77 51.406 47 61.486 17 71.565 87 81.645 57 91.725 27 101.804 97 111.884 67 121.964 37 132.044 07 142.123 77 152.203 47 162.283 17 172.362 87 182.442 57 192.522 27	2.015 94 12.095 64 22.175 34 32.255 04 42.334 74 52.414 44 62.494 14 72.573 84 82.653 54 92.733 24 102.812 94 112.892 64 122.972 34 133.052 04 143.131 74 153.211 44 163.291 14 173.370 84 183.450 54 193.530 24	3.023 91 13.103 61 23.183 31 33.263 01 43.342 71 53.422 41 63.502 11 73.581 81 83.661 51 93.741 21 103.820 91 113.900 61 123.980 31 134.060 01 144.139 71 154.219 41 164.299 11 174.378 81 184.458 51 194.538 21	4.031 88 14.111 58 24.191 28 34.270 98 44.350 68 54.430 38 64.510 08 74.589 78 84.669 48 94.749 18 104.828 88 114.908 58 124.988 28 135.067 98 145.147 68 155.227 38 165.307 08 175.386 78 185.466 48 195.546 18	5.039 85 15.119 55 25.199 25 35.278 95 45.358 65 55.438 35 65.518 05 75.597 75 85.677 45 95.757 15 105.836 85 115.916 55 125.996 25 136.075 95 146.155 65 156.235 35 166.315 05 176.394 75 186.474 45 196.554 15	6.047 82 16.127 52 26.207 22 36.286 92 46.366 62 56.446 32 66.526 02 76.605 72 86.685 42 96.765 12 106.844 82 116.924 52 127.004 22 137.083 92 147.163 62 157.243 32 167.323 02 177.402 72 187.482 42 197.562 12	7.055 79 17.135 49 27.215 19 37.294 89 47.374 59 57.454 29 67.533 99 77.613 69 87.693 39 97.773 09 107.852 79 117.932 49 128.012 19 138.091 89 148.171 59 158.251 29 168.330 99 178.410 69 188.490 39 198.570 09	8.063 76 18.143 46 28.223 16 38.302 86 48.382 56 58.462 26 68.541 96 78.621 66 88.701 36 98.781 06 108.860 76 118.940 46 129.020 16 139.099 86 149.179 56 159.259 26 169.338 96 179.418 66 189.498 36 199.578 06	9.071 46 19.151 16 29.231 86 39.310 56 49.390 26 59.470 96 69.549 66 79.629 36 89.709 06 99.789 76 109.868 46 119.948 16 130.028 86 140.107 56 150.187 26 160.267 96 170.346 66 180.426 36 190.506 06 200.586 76
6	C	Carbon	0 10 20 30 40 50 60 70 80 90	00.000 0 120.111 50 240.223 00 360.334 50 480.446 00 600.557 50 720.669 00 840.780 50 960.892 00 1081.003 50	12.011 15 132.122 65 252.234 15 372.345 65 492.457 15 612.568 65 732.680 15 852.791 65 972.903 15 1093.014 65	24.022 30 144.133 80 264.245 30 384.356 80 504.468 30 624.579 80 744.691 30 864.802 80 984.914 30 1105.025 80	36.033 45 156.144 95 276.256 45 396.367 95 516.479 45 636.590 95 756.702 45 876.813 95 996.925 45 1117.036 95	48.044 60 168.156 10 288.267 60 408.379 10 528.490 60 648.602 10 768.713 60 888.825 10 1008.936 60 1129.048 10	60.055 75 180.167 25 300.278 75 420.390 25 540.501 75 660.613 25 780.724 75 900.836 25 1020.947 75 1141.059 25	72.066 90 192.178 40 312.289 90 432.401 40 552.512 90 672.624 40 792.735 90 912.847 40 1032.958 90 1153.070 40	84.078 05 204.189 55 324.301 05 444.412 55 564.524 05 684.635 55 804.747 05 924.858 55 1044.970 05 1165.081 55	96.089 20 216.200 70 336.312 20 456.423 70 576.535 20 696.646 70 816.758 20 936.869 70 1056.981 20 1177.092 70	108.100 3 228.211 8 348.323 3 468.434 8 588.546 3 708.657 8 828.769 3 948.880 8 1068.992 3 1189.103 8
7	N	Nitrogen	0 10 20 30 40	00.000 0 140.067 0 280.134 0 420.201 0 560.268 0	14.006 7 154.073 7 294.140 7 434.207 7 574.274 7	28.013 4 168.080 4 308.147 4 448.214 4 588.281 4	42.020 1 182.087 1 322.154 1 462.221 1 602.288 1	56.026 8 196.093 8 336.160 8 476.227 8 616.294 8	70.033 5 210.100 5 350.167 5 490.234 5 630.301 5	84.040 2 224.107 2 364.174 2 504.241 2 644.308 2	98.046 9 238.113 9 378.180 9 518.247 9 658.314 9	112.053 6 252.120 6 392.187 6 532.254 6 672.321 6	126.060 3 266.127 3 406.194 3 546.261 3 686.328 3
8	O	Oxygen	0 10 20 30 40	00.000 0 159.994 0 319.988 0 479.982 0 639.976 0	15.999 4 175.993 4 335.987 4 495.981 4 655.975 4	31.998 8 191.992 8 351.986 8 511.980 8 671.974 8	47.998 2 207.992 2 367.986 2 527.980 2 687.974 2	63.997 6 223.991 6 383.985 6 543.979 6 703.973 6	79.997 0 239.991 0 399.985 0 559.979 0 719.973 0	95.996 4 255.990 4 415.984 4 575.978 4 735.972 4	111.995 8 271.989 8 431.983 8 591.977 8 751.971 8	127.995 2 287.989 2 447.983 2 607.977 2 767.971 2	143.994 6 303.988 6 463.982 6 623.976 6 783.970 6
9	F	Fluorine	0	00.000 0	18.998 4	37.996 8	56.995 2	75.993 6	94.992 0	113.990 4	132.988 8	151.987 2	170.985 6
11	Na	Sodium	0	00.000 0	22.989 8	45.979 6	68.969 4	91.959 2	114.949 0	137.938 8	160.928 6	183.918 4	206.908 2
12	Mg	Magnesium	0	00.000 0	24.305	48.610	72.915	97.220	121.525	145.830	170.135	194.440	218.745
13	Al	Aluminium	0	00.000 0	26.981 5	53.963 0	80.944 5	107.926 0	134.907 5	161.889 0	188.870 5	215.852 0	242.833 5
14	Si	Silicon	0	00.000 0	28.086	56.172	84.258	112.344	140.430	168.516	196.602	224.688	252.774
15	P	Phosphorus	0 10	00.000 0 309.738 0	30.973 8 340.711 8	61.947 6 371.685 6	92.921 4 402.659 4	123.895 2 433.633 2	154.869 0 464.607 0	185.842 8 495.580 8	216.816 6 526.554 6	247.790 4 557.528 4	278.764 2 588.502 2
16	S	Sulphur	0 10	00.000 0 320.640	32.064 352.704	64.128 384.768	96.192 416.832	128.256 448.896	160.320 480.960	192.384 513.024	224.448 545.088	256.512 577.152	288.576 609.216
17	Cl	Chlorine	0	00.000 0	35.453	70.906	106.359	141.812	177.265	212.718	248.171	283.624	319.077
19	K	Potassium	0	00.000 0	39.102	78.204	117.306	156.408	195.510	234.612	273.714	312.816	351.918
20	Ca	Calcium	0	00.00 0	40.08	80.16	120.24	160.32	200.40	240.48	280.56	320.64	360.72
25	Mn	Manganese	0	00.000 0	54.938	109.876	164.814	219.752	274.690	329.628	384.566	439.504	494.442
26	Fe	Iron	0	00.000 0	55.847	111.694	167.541	223.388	279.235	335.082	390.929	446.776	502.623
27	Co	Cobalt	0	00.000 0	58.933 2	117.866 4	176.799 6	235.732 8	294.666 0	353.599 2	412.532 4	471.465 6	530.398 8
29	Cu	Copper	0	00.00 0	63.546	127.092	190.638	254.184	317.730	381.276	444.822	508.368	571.914
30	Zn	Zinc	0	00.00 0	65.37	130.74	196.11	261.48	326.85	392.22	457.59	522.96	588.33
33	As	Arsenic	0	00.000 0	74.921 6	149.843 2	224.764 8	299.686 4	374.608 0	449.529 6	524.451 2	599.372 8	674.294 4
35	Br	Bromine	0	00.000 0	79.904	159.808	239.712	319.616	399.520	479.424	559.328	639.232	719.136
53	I	Iodine	0	000.000 0	126.904 4	253.808 8	380.713 2	507.617 6	634.522 0	761.426 4	888.330 8	1015.235 2	1142.139 6
	H ₂ O	Water(½H ₂ O = 9.007 67)	0 10	00.000 00 180.153 40	18.015 34 198.168 74	36.030 68 216.184 08	54.046 02 234.199 42	72.061 36 252.214 76	90.076 70 270.230 10	108.092 04 288.245 44	126.107 38 306.260 78	144.122 72 324.276 12	162.138 06 342.291 46
	CH ₂	Methylene	0 10 20 30 40	00.000 00 140.270 90 280.541 80 420.812 70 561.083 60	14.027 09 154.297 99 294.568 89 434.839 79 575.110 69	28.054 18 168.325 08 308.595 98 448.866 88 589.137 78	42.081 27 182.352 17 322.623 07 462.893 97 603.164 87	56.108 36 196.379 26 336.650 16 476.921 06 617.191 96	70.135 45 210.406 35 350.677 25 490.948 15 631.219 05	84.162 54 224.433 44 364.704 34 504.975 24 645.246 14	98.189 63 238.460 53 378.731 43 519.002 33 659.273 23	112.216 72 252.487 62 392.758 52 533.029 42 673.300 32	126.243 81 266.514 71 406.785 61 547.056 51 687.327 41
	CH ₃	Methyl	0 10 20	00.000 00 150.350 60 300.701 20	15.035 06 165.385 66 315.736 26	30.070 12 180.420 72 330.771 32	45.105 18 195.455 78 345.806 38	60.140 24 210.490 84 360.841 44	75.175 30 225.525 90 375.876 50	90.210 36 240.560 96 390.911 56	105.245 42 255.596 02 405.946 62	120.280 48 270.631 08 420.981 68	135.315 54 285.666 14 436.016 74
	NH ₄	Ammonium	0	00.000 00	18.038 58	36.077 16	54.115 74	72.154 32	90.192 90	108.231 48	126.270 06	144.308 64	162.347 22

Common chemical conversion factors

For converting	Factor	log ₁₀	For converting	Factor	log ₁₀
acetone into acetoacetic acid	1.758	0.2450	Acetoacetic acid into acetone	0.5689	0.7550-1
acetone into β-hydroxybutyric acid	1.792	0.2533	β-Hydroxybutyric acid into acetone	0.5579	0.7466-1
acetone into CaO	1.399	0.1458	CaO into Ca	0.7147	0.8541-1
acetone into NaCl	1.648	0.2170	NaCl into Cl	0.6066	0.7829-1
acetone into K ₂ O	1.205	0.0810	K ₂ O into K	0.8302	0.9192-1
acetone into MgO	1.658	0.2195	MgO into Mg	0.6032	0.7805-1
acetone into NaCl	2.542	0.4052	NaCl into Na	0.3934	0.5948-1
acetone into Na ₂ O	1.348	0.1297	Na ₂ O into Na	0.7419	0.8704-1
acetone into P ₂ O ₅	2.291	0.3600	P ₂ O ₅ into P	0.4364	0.6399-1
acetone into H ₃ PO ₄	3.164	0.5002	H ₃ PO ₄ into P	0.3161	0.4998-1
acetone into SO ₃	2.497	0.3974	SO ₃ into S	0.4005	0.6026-1
acetone into H ₂ SO ₄	3.059	0.4857	H ₂ SO ₄ into S	0.3269	0.5144-1
protein-N into protein	6.25	0.7959	Protein into protein-N	0.16	0.2041-1
ammonia-N into ammonia	1.216	0.0849	Ammonia into ammonia-N	0.8224	0.9151-1
creatine-N into creatine	3.121	0.4943	Creatine into creatine-N	0.3204	0.5057-1
creatinine-N into creatinine	2.692	0.4301	Creatinine into creatinine-N	0.3715	0.5700-1
urea-N into urea	2.144	0.3312	Urea into urea-N	0.4665	0.6689-1
uric acid-N into uric acid	3.001	0.4772	Uric acid into uric acid-N	0.3333	0.5228-1
lipid-P into phosphatides	23.5	1.3711	Lecithin into lipid-P	0.040	0.6021-2
lipid-P into lecithin	25	1.3979			

Conversion of concentration units

In clinical chemistry, concentration data for fluids should be related to the unit litre, those for solids to the unit kilogramme. The use of ambiguous units like 'g%', 'mg%', 'p.p.m.', etc. should be avoided since they do not make it clear whether the data relate to mass or to volume.

Conversion of mg/100 ml into mmol/l and vice versa

$$\text{mmol/l} = \frac{10 \times \text{mg/100 ml}}{\text{molecular weight}} = \frac{10000 \times \text{g/100 ml}}{\text{molecular weight}}$$

$$\text{mg/100 ml} = \frac{\text{mmol} \times \text{molecular weight}}{10}$$

Conversion of ml of gas/100 ml into mmol/l and vice versa at 0°C, 2.24 = millimolar normal volume of an ideal gas

$$\text{mmol/l} = \frac{\text{ml/100 ml}}{2.24}$$

$$\text{ml/100 ml} = 2.24 \times \text{mmol/l}$$

Conversion of mg/100 ml into mEq/l* and vice versa

$$\text{mEq/l} = \frac{10 \times \text{mg/100 ml} \times \text{valency}}{\text{molecular weight}}$$

$$\text{mg/100 ml} = \frac{\text{mEq/l} \times \text{molecular weight}}{10 \times \text{valency}}$$

* Cf. footnote on page 226.

Temperature variation of molarity and normality of aqueous solutions

The following conversion factors for temperatures deviating from the normal temperature of 20°C are for 0.1-N solutions and assume a coefficient of expansion for glass of 0.000027.

Temperature	Factor
14°C	1.0010
15°C	1.0009
16°C	1.0007
17°C	1.0006
18°C	1.0004
19°C	1.0002
20°C	1.0000
21°C	0.9998
22°C	0.9996
23°C	0.9994
24°C	0.9991
25°C	0.9989
26°C	0.9986
27°C	0.9983

Reference

* From a more extensive table in KOLTHOFF, I. M., *Die Mangananalyse*, part 2, Springer, Berlin, 1928, page 30.

The ICAO standard atmosphere is fundamentally defined in terms of an ideal gas assumed to be devoid of moisture, water vapour and dust. It is based on accepted standard values for the sea-level air, as follows:

Atmospheric pressure $p_0 = 1.01325 \times 10^5 \text{ N m}^{-2}$ ($= 760 \text{ torr}$)

Temperature $T_0 = 288.15 \text{ K}$ ($= 15^\circ \text{C}$)

Density $\rho_0 = 1.2250 \text{ kg m}^{-3}$

Acceleration due to gravity at 45° geographic latitude $g_0 = 9.80665 \text{ m s}^{-2}$

The relative molecular mass M (molecular weight) of air at sea level is calculated from the equation of state of a perfect gas

$$\rho = \frac{M p}{R T}$$

using the standard values for ρ_0 , p_0 , T_0 at sea level and for the molar gas constant R , which is based on the relative atomic mass (atomic weight; see page 226) of the nuclide $^{12}\text{C} = 12$.

Molar gas constant $R = 8.3143 \text{ J K}^{-1} \text{ mol}^{-1}$

Relative molecular mass of air at sea level $M_0 = 28.9644$

Note that for the altitudes tabulated below the mean relative molecular mass of air is assumed to be the same as at sea level (M_0).

Composition of clean, dry atmospheric air near sea level

Gas	Relative molecular mass	vol %	Gas	Relative molecular mass	vol %
N_2	28.0134	78.084	CH_4	16.04303	*0.0002
O_2	31.9988	20.9476	N_2O	44.0128	0.00005
Ar	39.948	0.934	O_3	47.9982	*Summer 0-0.00
CO_2	44.00995	*0.0314	SO_2	64.0628	*Winter 0-0.00
Ne	20.183	0.001818	NO_2	46.0055	*0-0.00002
He	4.0026	0.000524	NH_3	17.03061	*0 to traces
Kr	83.80	0.000114	CO	28.01055	*0 to traces
Xe	131.30	0.0000087	I_2	253.8088	*0-0.000001
H_2	2.01594	0.00005			

* The content of these gases may undergo significant variations from time to time or from place to place relative to the normal indicated for the

Reference

¹ From the *Manual of the ICAO Standard Atmosphere*, 2nd ed., International Civil Aviation Organization, Montreal, 1964. Reproduced by kind permission of the publishers.

Geo-metric altitude (m)	Temperature ($^\circ\text{C}$)	Atmospheric pressure		p/p_0	Boiling point of water* ($^\circ\text{C}$)	Density (kg m^{-3})	ρ/ρ_0	Velocity of sound (m s^{-1})	Dynamic viscosity (N s m^{-2})	Thermal conductivity ($\text{kcal m}^{-1} \text{s}^{-1} \text{deg}^{-1}$)	Geo-metric altitude (ft)
		mbar	torr								
-1000	21.501	1.13931+3	8.54554+2	1.12441+0	103.31	1.3470+0	1.0996+0	344.111	1.8206-5	6.1748-6	-3281
-950	21.176	1.13272	8.49610	1.11791	103.15	1.3407	1.0945	343.921	1.8190	6.1687	-3116
-900	20.851	1.12616	8.44689	1.11143	102.98	1.3344	1.0893	343.731	1.8175	6.1626	-2952
-850	20.526	1.11963	8.39792	1.10499	102.81	1.3281	1.0842	343.541	1.8159	6.1566	-2788
-800	20.201	1.11313	8.34917	1.09858	102.65	1.3219	1.0791	343.351	1.8144	6.1505	-2624
-750	19.876	1.10666	8.30066	1.09219	102.48	1.3157	1.0740	343.161	1.8128	6.1444	-2460
-700	19.550	1.10023	8.25237	1.08584	102.32	1.3095	1.0690	342.970	1.8113	6.1383	-2296
-650	19.225	1.09382	8.20432	1.07952	102.15	1.3033	1.0639	342.780	1.8097	6.1323	-2132
-600	18.900	1.08744	8.15649	1.07322	101.99	1.2971	1.0589	342.589	1.8081	6.1262	-1968
-550	18.575	1.08110	8.10889	1.06696	101.83	1.2910	1.0539	342.399	1.8066	6.1201	-1804
-500	18.250	1.07478+3	8.06151+2	1.06073+0	101.66	1.2849+0	1.0489+0	342.208	1.8050-5	6.1140-6	-1640
-450	17.925	1.06849	8.01436	1.05452	101.49	1.2788	1.0439	342.017	1.8035	6.1079	-1476
-400	17.600	1.06224	7.96743	1.04835	101.32	1.2727	1.0390	341.826	1.8019	6.1018	-1312
-350	17.275	1.05601	7.92073	1.04220	101.16	1.2667	1.0340	341.635	1.8003	6.0957	-1148
-300	16.950	1.04981	7.87425	1.03609	100.99	1.2607	1.0291	341.443	1.7988	6.0896	-984
-250	16.625	1.04365	7.82799	1.03000	100.82	1.2547	1.0242	341.252	1.7972	6.0835	-820
-200	16.300	1.03751	7.78195	1.02394	100.66	1.2487	1.0193	341.061	1.7956	6.0774	-656
-150	15.975	1.03140	7.73614	1.01791	100.49	1.2427	1.0145	340.869	1.7941	6.0713	-492
-100	15.650	1.02532	7.69054	1.01191	100.33	1.2368	1.0096	340.678	1.7925	6.0652	-328
-50	15.325	1.01927	7.64516	1.00594	100.16	1.2309	1.0048	340.486	1.7909	6.0591	-164
0	15.000	1.01325+3	7.60000+2	1.00000+0	100.00	1.2250+0	1.0000+0	340.294	1.7894-5	6.0530-6	0
50	14.675	1.00726	7.55505	0.994086-1	99.83	1.2191	0.99521-1	340.102	1.7878	6.0469	164
100	14.350	1.00129	7.51032	0.988201	99.66	1.2133	0.99044	339.910	1.7862	6.0408	328
150	14.025	0.995360+2	7.46581	0.982344	99.50	1.2075	0.98568	339.718	1.7847	6.0347	492
200	13.700	0.989454	7.42151	0.976515	99.33	1.2017	0.98094	339.525	1.7831	6.0286	656
250	13.375	0.983576	7.37743	0.970714	99.17	1.1959	0.97622	339.333	1.7815	6.0225	820
300	13.050	0.977727	7.33356	0.964942	99.00	1.1901	0.97152	339.141	1.7800	6.0164	984
350	12.725	0.971906	7.28990	0.959197	98.83	1.1844	0.96683	338.948	1.7784	6.0102	1148
400	12.400	0.966114	7.24645	0.953480	98.67	1.1786	0.96216	338.755	1.7768	6.0041	1312
450	12.075	0.960349	7.20321	0.947791	98.50	1.1729	0.95751	338.562	1.7752	5.9980	1476
500	11.750	0.954612+2	7.16018+2	0.942129-1	98.33	1.1673+0	0.95288-1	338.370	1.7737-5	5.9919-6	1640
550	11.425	0.948904	7.11736	0.936495	98.17	1.1616	0.94826	338.177	1.7721	5.9858	1804
600	11.100	0.943223	7.07475	0.930889	98.00	1.1559	0.94366	337.983	1.7705	5.9796	1968
650	10.775	0.937570	7.03235	0.925309	97.84	1.1504	0.93908	337.790	1.7689	5.9735	2132
700	10.450	0.931944	6.99015	0.919757	97.67	1.1448	0.93451	337.597	1.7673	5.9674	2296
750	10.125	0.926346	6.94816	0.914232	97.50	1.1392	0.92996	337.403	1.7658	5.9612	2460
800	9.800	0.920775	6.90638	0.908734	97.34	1.1337	0.92543	337.210	1.7642	5.9551	2624
850	9.475	0.915231	6.86480	0.903263	97.17	1.1281	0.92092	337.016	1.7626	5.9490	2788
900	9.150	0.909714	6.82342	0.897818	97.00	1.1226	0.91642	336.822	1.7610	5.9428	2952
950	8.825	0.904225	6.78225	0.892401	96.84	1.1171	0.91194	336.629	1.7594	5.9367	3116
1000	8.501	0.898762+2	6.74127+2	0.887009-1	96.68	1.1117+0	0.90748-1	336.435	1.7579-5	5.9305-6	3280
1050	8.176	0.893327	6.70050	0.881645	96.50	1.1062	0.90303	336.240	1.7563	5.9244	3444
1100	7.851	0.887918	6.65993	0.876307	96.34	1.1008	0.89860	336.046	1.7547	5.9182	3608
1150	7.526	0.882535	6.61956	0.870995	96.18	1.0954	0.89419	335.852	1.7531	5.9121	3772
1200	7.201	0.877180	6.57939	0.865709	96.00	1.0900	0.88979	335.657	1.7515	5.9059	3936
1250	6.877	0.871850	6.53941	0.860449	95.84	1.0846	0.88541	335.463	1.7499	5.8998	4100
1300	6.552	0.866547	6.49964	0.855215	95.68	1.0793	0.88105	335.268	1.7483	5.8936	4264
1350	6.227	0.861270	6.46006	0.850008	95.51	1.0740	0.87670	335.074	1.7467	5.8875	4428
1400	5.902	0.856020	6.42068	0.844826	95.34	1.0687	0.87237	334.879	1.7451	5.8813	4592
1450	5.577	0.850795	6.38149	0.839669	95.18	1.0634	0.86806	334.684	1.7436	5.8752	4756
1500	5.252	0.845596+2	6.34249+2	0.834539-1	95.01	1.0581+0	0.86376-1	334.489	1.7420-5	5.8690-6	4920
1550	4.927	0.840423	6.30369	0.829433	94.84	1.0529	0.85948	334.293	1.7404	5.8628	5084
1600	4.603	0.835276	6.26509	0.824354	94.68	1.0476	0.85521	334.098	1.7388	5.8567	5248
1650	4.278	0.830155	6.22667	0.819299	94.51	1.0424	0.85096	333.903	1.7372	5.8505	5412
1700	3.953	0.825059	6.18845	0.814270	94.34	1.0372	0.84673	333.707	1.7356	5.8443	5576
1750	3.628	0.819988	6.15042	0.809265	94.17	1.0321	0.84252	333.511	1.7340	5.8382	5740
1800	3.303	0.814943	6.11258	0.804286	94.01	1.0269	0.83832	333.316	1.7324	5.8320	5904
1850	2.978	0.809923	6.07492	0.799332	93.84	1.0218	0.83413	333.120	1.7308	5.8258	6068
1900	2.654	0.804928	6.03746	0.794402	93.68	1.0167	0.82996	332.924	1.7292	5.8197	6232
1950	2.329	0.799958	6.00018	0.789498	93.51	1.0116	0.82581	332.728	1.7276	5.8135	6396
2000	2.004	0.795014+2	5.96309+2	0.784618-1	93.34	1.0066+0	0.82168-1	332.532	1.7260-5	5.8073-6	6560
2050	1.679	0.790094	5.92619	0.779762	93.17	1.0015	0.81756	332.335	1.7244	5.8011	6724
2100	1.355	0.785199	5.88947	0.774931	93.01	0.99648-1	0.81345	332.139	1.7228	5.7949	6888
2150	1.030	0.780328	5.85294	0.770124	92.84	0.99147	0.80936	331.942	1.7212	5.7887	7052
2200	0.705	0.775482	5.81659	0.765341	92.67	0.98648	0.80529	331.746	1.7196	5.7826	7216
2250	0.380	0.770661	5.78043	0.760583	92.51	0.98151	0.80124	331.549	1.7180	5.7764	7380
2300	0.055	0.765863	5.74445	0.755849	92.34	0.97656	0.79719	331.352	1.7164	5.7702	7544
2350	-0.269	0.761091	5.70865	0.751138	92.17	0.97163	0.79317	331.155	1.7147	5.7640	7708
2400	-0.594	0.756342	5.67303	0.746452	92.01	0.96672	0.78916	330.958	1.7131	5.7578	7872
2450	-0.919	0.751618	5.63760	0.741789	91.84	0.96183	0.78517	330.761	1.7115	5.7516	8036

* Interpolated by the editors from the table on page 257.

Geo- metric altitude (m)	Temper- ature (°C)	Atmospheric pressure		ρ/ρ_0	Boiling point of water ^a (°C)	Density (kg m ⁻³)	σ/σ_0	Velocity of sound (m s ⁻¹)	Dynamic viscosity (N s m ⁻²)	Thermal conductivity (kcal m ⁻¹ s ⁻¹ deg ⁻¹)	Geo- metric altitude (ft)
		mbar	torr								
2500				-1	91 67	9 5695-1	7 8119-1	338 563	1 7099-5	5 7454-6	8202.1
2510					91 51	9 5210	7 7722	330 366	1 7015	5 7492-6	8246.1
2520					91 34	9 4726	7 7328	330 168	1 7087	5 7530	8530.2
2530					91 17	9 4245	7 6934	329 971	1 7051	5 7268	8694.2
2540					91 01	9 3765	7 6543	329 773	1 7035	5 7206	8858.3
2550					90 84	9 3287	7 6153	329 575	1 7019	5 7144	9022.3
2560					90 67	9 2811	7 5764	329 377	1 7002	5 7082	9186.4
2570					90 50	9 2337	7 5377	329 179	1 6986	5 7019	9350.4
2580					90 33	9 1864	7 4991	328 980	1 6970	5 6957	9514.4
2590					90 17	9 1394	7 4607	328 782	1 6954	5 6895	9678.5
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ICAO Standard Atmosphere

Geo- metric altitude (m)	Temper- ature (°C)	Atmospheric pressure		p/p_0	Boiling point of water* (°C)	Density (kg m ⁻³)	ρ/ρ_0	Velocity of sound (m s ⁻¹)	Dynamic viscosity (N s m ⁻²)	Thermal conductivity (kcal m ⁻¹ s ⁻¹ deg ⁻¹)	Geo- metric altitude (ft)
		mbar	torr								
7500	-33.693	3.82996+2	2.87271+2	3.77988-1	74.84	5.5719-1	4.5485-1	310.212	1.5442-5	5.1160-6	24606.3
7550	-34.017	3.80279	2.85232	3.75306	74.68	5.5399	4.5224	310.002	1.5425	5.1096	24770.3
7600	-34.341	3.77577	2.83206	3.72639	74.51	5.5080	4.4963	309.792	1.5408	5.1032	24934.4
7650	-34.665	3.74890	2.81191	3.69988	74.34	5.4762	4.4704	309.582	1.5391	5.0968	25098.4
7700	-34.989	3.72219	2.79187	3.67352	74.17	5.4446	4.4446	309.371	1.5374	5.0904	25262.5
7750	-35.313	3.69564	2.77196	3.64731	74.00	5.4131	4.4189	309.160	1.5357	5.0840	25426.5
7800	-35.638	3.66924	2.75215	3.62125	73.83	5.3818	4.3933	308.950	1.5340	5.0776	25590.6
7850	-35.962	3.64299	2.73247	3.59535	73.66	5.3506	4.3678	308.739	1.5323	5.0712	25754.6
7900	-36.286	3.61689	2.71289	3.56960	73.49	5.3196	4.3425	308.528	1.5305	5.0648	25918.6
7950	-36.610	3.59095	2.69343	3.54399	73.32	5.2886	4.3173	308.317	1.5288	5.0584	26082.7
8000	-36.935	3.56516+2	2.67409+2	3.51854-1	73.15	5.2579-1	4.2921-1	308.105	1.5271-5	5.0520-6	26246.7
8050	-37.259	3.53952	2.65486	3.49323	72.97	5.2272	4.2671	307.894	1.5254	5.0456	26410.8
8100	-37.583	3.51403	2.63574	3.46807	72.80	5.1967	4.2422	307.682	1.5237	5.0392	26574.8
8150	-37.907	3.48868	2.61673	3.44306	72.63	5.1663	4.2174	307.470	1.5220	5.0328	26738.8
8200	-38.231	3.46349	2.59783	3.41820	72.47	5.1361	4.1927	307.258	1.5202	5.0264	26902.9
8250	-38.555	3.43845	2.57905	3.39348	72.29	5.1060	4.1682	307.046	1.5185	5.0200	27066.9
8300	-38.880	3.41355	2.56037	3.36891	72.12	5.0761	4.1437	306.834	1.5168	5.0135	27231.0
8350	-39.204	3.38880	2.54181	3.34448	71.96	5.0462	4.1194	306.622	1.5151	5.0071	27395.0
8400	-39.528	3.36419	2.52335	3.32020	71.78	5.0165	4.0951	306.409	1.5134	5.0007	27559.1
8450	-39.852	3.33973	2.50500	3.29606	71.62	4.9870	4.0710	306.197	1.5116	4.9943	27723.1
8500	-40.176	3.31541+2	2.48677+2	3.27206-1	71.44	4.9576-1	4.0470-1	305.984	1.5099-5	4.9878-6	27887.1
8550	-40.500	3.29121	2.46861	3.24849	71.27	4.9281	4.0221	305.772	1.5082	4.9814	28051.2
8600	-40.824	3.26721	2.45061	3.22449	71.11	4.8991	3.9993	305.558	1.5065	4.9750	28215.2
8650	-41.148	3.24321	2.43261	3.20049	70.94	4.8701	3.9744	305.346	1.5048	4.9686	28379.3
8700	-41.472	3.21921	2.41461	3.17649	70.78	4.8412	3.9495	305.134	1.5031	4.9622	28543.3
8750	-41.796	3.19521	2.39661	3.15249	70.62	4.8122	3.9246	304.922	1.5014	4.9558	28707.4
8800	-42.120	3.17121	2.37861	3.12849	70.46	4.7833	3.8997	304.710	1.5000	4.9494	28871.4
8850	-42.444	3.14721	2.36061	3.10449	70.30	4.7543	3.8748	304.498	1.4983	4.9430	29035.5
8900	-42.768	3.12321	2.34261	3.08049	70.14	4.7254	3.8499	304.286	1.4966	4.9366	29199.5
8950	-43.092	3.09921	2.32461	3.05649	69.98	4.6964	3.8250	304.074	1.4949	4.9302	29363.6
9000	-43.416	3.07521	2.30661	3.03249	69.82	4.6675	3.8001	303.862	1.4932	4.9238	29527.6
9050	-43.740	3.05121	2.28861	3.00849	69.66	4.6385	3.7752	303.650	1.4915	4.9174	29691.7
9100	-44.064	3.02721	2.27061	2.98449	69.50	4.6096	3.7503	303.438	1.4898	4.9110	29855.7
9150	-44.388	3.00321	2.25261	2.96049	69.34	4.5806	3.7254	303.226	1.4881	4.9046	30019.8
9200	-44.712	2.97921	2.23461	2.93649	69.18	4.5517	3.7005	303.014	1.4864	4.8982	30183.8
9250	-45.036	2.95521	2.21661	2.91249	69.02	4.5227	3.6756	302.802	1.4847	4.8918	30347.9
9300	-45.360	2.93121	2.19861	2.88849	68.86	4.4938	3.6507	302.590	1.4830	4.8854	30511.9
9350	-45.684	2.90721	2.18061	2.86449	68.70	4.4648	3.6258	302.378	1.4813	4.8790	30676.0
9400	-46.008	2.88321	2.16261	2.84049	68.54	4.4359	3.6009	302.166	1.4796	4.8726	30840.0
9450	-46.332	2.85921	2.14461	2.81649	68.38	4.4069	3.5760	301.954	1.4779	4.8662	31004.1
9500	-46.656	2.83521	2.12661	2.79249	68.22	4.3780	3.5511	301.742	1.4762	4.8598	31168.1
9550	-46.980	2.81121	2.10861	2.76849	68.06	4.3490	3.5262	301.530	1.4745	4.8534	31332.2
9600	-47.304	2.78721	2.09061	2.74449	67.90	4.3201	3.5013	301.318	1.4728	4.8470	31496.2
9650	-47.628	2.76321	2.07261	2.72049	67.74	4.2911	3.4764	301.106	1.4711	4.8406	31660.3
9700	-47.952	2.73921	2.05461	2.69649	67.58	4.2622	3.4515	300.894	1.4694	4.8342	31824.3
9750	-48.276	2.71521	2.03661	2.67249	67.42	4.2332	3.4266	300.682	1.4677	4.8278	31988.4
9800	-48.600	2.69121	2.01861	2.64849	67.26	4.2043	3.4017	300.470	1.4660	4.8214	32152.4
9850	-48.924	2.66721	2.00061	2.62449	67.10	4.1753	3.3768	300.258	1.4643	4.8150	32316.5
9900	-49.248	2.64321	1.98261	2.60049	66.94	4.1464	3.3519	300.046	1.4626	4.8086	32480.5
10000	-49.572	2.61921	1.96461	2.57649	66.78	4.1174	3.3270	299.834	1.4609	4.8022	32644.6
10050	-49.896	2.59521	1.94661	2.55249	66.62	4.0885	3.3021	299.622	1.4592	4.7958	32808.6
10100	-50.220	2.57121	1.92861	2.52849	66.46	4.0595	3.2772	299.410	1.4575	4.7894	32972.7
10150	-50.544	2.54721	1.91061	2.50449	66.30	4.0306	3.2523	299.198	1.4558	4.7830	33136.7
10200	-50.868	2.52321	1.89261	2.48049	66.14	4.0016	3.2274	298.986	1.4541	4.7766	33300.8
10250	-51.192	2.49921	1.87461	2.45649	65.98	3.9727	3.2025	298.774	1.4524	4.7702	33464.8
10300	-51.516	2.47521	1.85661	2.43249	65.82	3.9437	3.1776	298.562	1.4507	4.7638	33628.9
10350	-51.840	2.45121	1.83861	2.40849	65.66	3.9148	3.1527	298.350	1.4490	4.7574	33792.9
10400	-52.164	2.42721	1.82061	2.38449	65.50	3.8858	3.1278	298.138	1.4473	4.7510	33957.0
10450	-52.488	2.40321	1.80261	2.36049	65.34	3.8569	3.1029	297.926	1.4456	4.7446	34121.0
10500	-52.812	2.37921	1.78461	2.33649	65.18	3.8279	3.0780	297.714	1.4439	4.7382	34285.1
10550	-53.136	2.35521	1.76661	2.31249	65.02	3.7990	3.0531	297.502	1.4422	4.7318	34449.1
10600	-53.460	2.33121	1.74861	2.28849	64.86	3.7700	3.0282	297.290	1.4405	4.7254	34613.2
10650	-53.784	2.30721	1.73061	2.26449	64.70	3.7411	3.0033	297.078	1.4388	4.7190	34777.2
10700	-54.108	2.28321	1.71261	2.24049	64.54	3.7121	2.9784	296.866	1.4371	4.7126	34941.3
10750	-54.432	2.25921	1.69461	2.21649	64.38	3.6832	2.9535	296.654	1.4354	4.7062	35105.3
10800	-54.756	2.23521	1.67661	2.19249	64.22	3.6542	2.9286	296.442	1.4337	4.7000	35269.4
10850	-55.080	2.21121	1.65861	2.16849	64.06	3.6253	2.9037	296.230	1.4320	4.6936	35433.4
10900	-55.404	2.18721	1.64061	2.14449	63.90	3.5963	2.8788	296.018	1.4303	4.6872	35597.5
10950	-55.728	2.16321	1.62261	2.12049	63.74	3.5674	2.8539	295.806	1.4286	4.6808	35761.5
11000	-56.052	2.13921	1.60461	2.09649	63.58	3.5384	2.8290	295.594	1.4269	4.6744	35925.6
11050	-56.376	2.11521	1.58661	2.07249	63.42	3.5095	2.8041	295.382	1.4252	4.6680	36089.6
11100	-56.700	2.09121	1.56861	2.04849	63.26	3.4805	2.7792	295.170	1.4235	4.6616	36253.7
11150	-57.024	2.06721	1.55061	2.02449	63.10	3.4516	2.7543	294.958	1.4218	4.6552	36417.7
11200	-57.348	2.04321	1.53261	2.00049	62.94	3.4226	2.7294	294.746	1.4201	4.6488	36581.8
11250	-57.672	2.01921	1.51461	1.97649	62.78	3.3937	2.7045	294.534	1.4184	4.6424	36745.8
11300	-57.996	1.99521	1.49661	1.95249	62.62	3.3647	2.6796	294.322	1.4167	4.6360	36909.9
11350	-58.320	1.97121	1.47861	1.92849	62.46	3.3358	2.6547	294.110	1.4150	4.6296	37073.9
11400	-58.644	1.94721	1.46061	1.90449	62.30	3.3068	2.6298	293.898	1.4133	4.6232	37238.0
11450	-58.968	1.92321	1.44261	1.88049	62.14	3.2779	2.6049	293.686	1.4116	4.6168	37402.0
11500	-59.292	1.89921	1.42461	1.85649	61.98	3.2489	2.5800	293.474	1.4099	4.6104	37566.1
11550	-59.616	1.87521	1.40661	1.83249	61.82	3.2199	2.5551	293.262	1.4082	4.6040	37730.1
11600	-59.940	1.85121	1.38861	1.80849	61.66	3.1910	2.5302	293.050	1.4065	4.5976	37894.2
11650	-60.264	1.82721	1.37061	1.78449	61.50	3.1620	2.5053	292.838	1.4048	4.5912	38058.2
11700	-60.588	1.80321	1.35261	1.76049	61.34	3.1331	2.4804	292.626	1.4031	4.5848	38222.3
11750	-60.912	1.77921	1.33461	1.73649	61.18	3.1041	2.4555	292.414</			

The correction factor f_2 is calculated from the formula $f_2 = 1 - \frac{(\beta - \alpha) t}{1 + \beta t}$ where

Brass scale		Barometer reading β_0 in mm Hg																Correction factor f_2
		600	610	620	630	640	650	660	670	680	690	700	710	720	730	740	750	
meter temperature °C		Amount $\Delta\alpha$ in millimetres to be subtracted																
1																		0.999 837
2																		999 573
3																		999 520
4																		999 346
5																		0.999 184
6																		999 021
7																		998 858
8																		998 695
9																		998 532
10																		0.998 369
11																		998 206
12																		998 044
13																		997 881
14																		997 718
15																		0.997 556
16																		997 393
17																		997 231
18																		997 068
19																		996 906
20																		0.996 744
21																		996 582
22																		996 420
23																		996 258
24																		996 095
25																		0.995 933
26																		995 772
27																		995 610
28																		995 448
29																		995 286
30																		0.995 125
31																		994 963
32																		994 801
33																		994 640
34																		994 479
35																		0.994 317
36																		994 156
37																		993 995
38																		993 833
39																		993 672
40		5.89	5.96	4.02	4.09	4.15	4.22	4.28	4.35	4.41	4.48	4.54	4.61	4.67	4.74	4.80	4.87	0.993 511

Glass scale																		Correction factor f_2
1																		0.999 827
2																		999 658
3																		999 480
4																		999 307
5																		0.999 134
6																		998 961
7																		998 788
8																		998 616
9																		998 443
10																		0.998 270
11																		998 098
12																		997 925
13																		997 752
14																		997 580
15																		0.997 407
16																		997 235
17																		997 063
18																		996 891
19																		996 719
20																		0.996 547
21																		996 375
22																		996 203
23																		996 031
24																		995 859
25																		0.995 687
26																		995 514
27																		995 344
28																		995 170
29																		995 001
30																		0.994 828
31																		994 658
32																		994 487
33																		994 315
34																		994 144
35																		0.993 974
36																		993 802
37																		993 631
38																		993 460
39																		993 289
40		4.13	4.20	4.27	4.34	4.40	4.47	4.54	4.61	4.68	4.75	4.82	4.89	4.96	5.02	5.09	5.15	0.993 118

Saturation pressure of water vapour below 0°C over ice

microbar (μb) [†]											0.001 torr*										
°C	9	8	7	6	5	4	3	2	1	0	°C	9	8	7	6	5	4	3	2	1	0
-90	0.017	0.021	0.026	0.031	0.038	0.046	0.055	0.067	0.080	0.097	-90	0.013	0.016	0.019	0.023	0.028	0.034	0.042	0.050	0.060	0.07
-80	0.116	0.139	0.166	0.198	0.235	0.280	0.332	0.393	0.464	0.547	-80	0.087	0.104	0.124	0.148	0.176	0.210	0.249	0.294	0.348	0.41
-70	0.644	0.758	0.889	1.042	1.220	1.425	1.662	1.936	2.252	2.615	-70	0.483	0.568	0.667	0.782	0.915	1.07	1.25	1.45	1.69	1.96
-60	3.032	3.511	4.060	4.688	5.406	6.225	7.159	8.223	9.432	10.80	-60	2.27	2.63	3.05	3.52	4.05	4.67	5.37	6.17	7.07	8.10
-50	12.36	14.13	16.12	18.38	20.92	23.80	27.03	30.67	34.76	39.35	-50	9.27	10.60	12.09	13.79	15.69	17.85	20.27	23.00	26.07	29.51
-40	44.49	50.26	56.71	63.93	71.98	80.97	90.98	102.1	114.5	128.3	-40	33.37	37.70	42.54	47.95	53.99	60.73	68.24	76.58	85.89	96.23
-30	143.6	160.6	179.4	200.2	223.3	248.8	276.9	307.9	342.1	379.8	-30	107.7	120.5	134.6	150.2	167.5	186.6	207.7	230.9	256.6	284.9

millibar (mb) [†]											torr*										
°C	.9	.8	.7	.6	.5	.4	.3	.2	.1	.0	°C	.9	.8	.7	.6	.5	.4	.3	.2	.1	.0
-29	0.384	0.388	0.392	0.396	0.400	0.404	0.408	0.413	0.417	0.421	-29	0.288	0.291	0.294	0.297	0.300	0.303	0.306	0.310	0.313	0.316
-28	0.426	0.430	0.435	0.439	0.444	0.448	0.453	0.457	0.462	0.467	-28	0.319	0.323	0.326	0.329	0.333	0.336	0.340	0.343	0.347	0.350
-27	0.472	0.477	0.481	0.486	0.491	0.496	0.501	0.507	0.512	0.517	-27	0.354	0.357	0.361	0.365	0.369	0.372	0.376	0.380	0.384	0.388
-26	0.522	0.528	0.533	0.538	0.544	0.549	0.555	0.561	0.566	0.572	-26	0.392	0.396	0.400	0.404	0.408	0.412	0.416	0.421	0.425	0.430
-25	0.578	0.584	0.590	0.596	0.602	0.608	0.614	0.620	0.626	0.632	-25	0.433	0.438	0.442	0.447	0.451	0.456	0.460	0.465	0.470	0.474
-24	0.639	0.645	0.652	0.658	0.665	0.671	0.678	0.685	0.692	0.699	-24	0.479	0.484	0.488	0.494	0.499	0.504	0.509	0.514	0.519	0.524
-23	0.706	0.713	0.720	0.727	0.734	0.741	0.749	0.756	0.763	0.771	-23	0.529	0.534	0.540	0.545	0.551	0.556	0.561	0.567	0.573	0.578
-22	0.779	0.786	0.794	0.802	0.810	0.818	0.826	0.834	0.842	0.850	-22	0.584	0.590	0.596	0.601	0.607	0.613	0.619	0.625	0.632	0.638
-21	0.859	0.867	0.875	0.884	0.893	0.901	0.910	0.919	0.928	0.937	-21	0.644	0.650	0.657	0.663	0.670	0.676	0.683	0.689	0.696	0.703
-20	0.946	0.955	0.965	0.974	0.983	0.993	1.002	1.012	1.022	1.032	-20	0.710	0.717	0.723	0.731	0.738	0.745	0.752	0.759	0.767	0.774
-19	1.042	1.052	1.062	1.072	1.082	1.092	1.103	1.114	1.124	1.135	-19	0.782	0.789	0.797	0.804	0.812	0.819	0.827	0.836	0.843	0.851
-18	1.146	1.157	1.168	1.179	1.190	1.201	1.213	1.225	1.236	1.248	-18	0.860	0.868	0.876	0.884	0.893	0.901	0.910	0.919	0.927	0.936
-17	1.260	1.272	1.284	1.296	1.308	1.320	1.333	1.345	1.358	1.371	-17	0.945	0.954	0.963	0.972	0.981	0.990	1.000	1.009	1.019	1.028
-16	1.384	1.397	1.410	1.424	1.437	1.451	1.464	1.478	1.492	1.506	-16	1.038	1.048	1.058	1.068	1.078	1.088	1.098	1.109	1.119	1.130
-15	1.520	1.534	1.548	1.562	1.577	1.591	1.607	1.622	1.637	1.652	-15	1.140	1.151	1.161	1.172	1.183	1.194	1.205	1.217	1.228	1.239
-14	1.667	1.683	1.698	1.714	1.730	1.746	1.762	1.778	1.795	1.811	-14	1.250	1.262	1.274	1.286	1.298	1.310	1.322	1.334	1.346	1.358
-13	1.827	1.844	1.861	1.878	1.895	1.913	1.930	1.948	1.966	1.984	-13	1.370	1.383	1.396	1.409	1.421	1.435	1.448	1.461	1.475	1.488
-12	2.002	2.020	2.039	2.057	2.076	2.095	2.114	2.133	2.153	2.172	-12	1.502	1.515	1.529	1.543	1.557	1.571	1.586	1.600	1.615	1.629
-11	2.191	2.211	2.231	2.251	2.271	2.292	2.313	2.334	2.355	2.376	-11	1.643	1.658	1.673	1.688	1.703	1.719	1.735	1.751	1.766	1.782
-10	2.397	2.419	2.440	2.462	2.484	2.506	2.529	2.551	2.574	2.597	-10	1.798	1.814	1.830	1.847	1.863	1.880	1.897	1.913	1.931	1.948
-9	2.620	2.644	2.667	2.691	2.715	2.739	2.763	2.787	2.812	2.837	-9	1.965	1.983	2.000	2.018	2.036	2.054	2.072	2.090	2.109	2.125
-8	2.862	2.888	2.913	2.939	2.965	2.991	3.017	3.043	3.070	3.097	-8	2.147	2.166	2.185	2.204	2.224	2.243	2.263	2.282	2.303	2.323
-7	3.124	3.152	3.180	3.208	3.236	3.264	3.292	3.321	3.350	3.379	-7	2.343	2.364	2.385	2.406	2.427	2.448	2.469	2.491	2.513	2.534
-6	3.409	3.438	3.468	3.499	3.529	3.560	3.591	3.622	3.653	3.685	-6	2.557	2.579	2.601	2.624	2.647	2.670	2.693	2.717	2.740	2.764
-5	3.717	3.748	3.781	3.813	3.846	3.879	3.913	3.947	3.981	4.015	-5	2.788	2.811	2.836	2.860	2.885	2.909	2.935	2.960	2.986	3.011
-4	4.049	4.084	4.119	4.154	4.190	4.226	4.262	4.298	4.335	4.372	-4	3.037	3.063	3.090	3.116	3.143	3.170	3.197	3.224	3.252	3.279
-3	4.409	4.447	4.485	4.523	4.561	4.600	4.638	4.678	4.717	4.757	-3	3.307	3.336	3.364	3.393	3.421	3.450	3.479	3.509	3.538	3.568
-2	4.797	4.838	4.878	4.920	4.961	5.003	5.045	5.087	5.130	5.173	-2	3.598	3.629	3.659	3.690	3.721	3.753	3.784	3.816	3.848	3.880
-1	5.217	5.260	5.305	5.349	5.394	5.439	5.485	5.530	5.577	5.623	-1	3.913	3.945	3.979	4.012	4.046	4.080	4.114	4.148	4.183	4.218
0	5.670	5.717	5.764	5.812	5.860	5.909	5.958	6.007	6.057	6.107	0	4.253	4.288	4.323	4.359	4.395	4.432	4.469	4.506	4.543	4.581

Saturation pressure of water vapour below 0°C over water

millibar (mb) [†]											torr*										
°C	.9	.8	.7	.6	.5	.4	.3	.2	.1	.0	°C	.9	.8	.7	.6	.5	.4	.3	.2	.1	.0
-14	1.928	1.944	1.960	1.976	1.992	2.009	2.025	2.042	2.059	2.076	-14	1.446	1.458	1.470	1.482	1.494	1.507	1.519	1.532	1.544	1.557
-13	2.093	2.110	2.127	2.144	2.162	2.180	2.197	2.215	2.233	2.252	-13	1.570	1.582	1.595	1.608	1.622	1.635	1.648	1.662	1.675	1.689
-12	2.270	2.288	2.307	2.326	2.345	2.364	2.383	2.402	2.421	2.441	-12	1.703	1.716	1.730	1.744	1.759	1.773	1.787	1.802	1.816	1.831
-11	2.461	2.480	2.500	2.521	2.541	2.561	2.582	2.602	2.623	2.644	-11	1.846	1.861	1.876	1.891	1.906	1.921	1.936	1.952	1.968	1.983
-10	2.666	2.687	2.708	2.730	2.752	2.774	2.796	2.818	2.840	2.863	-10	1.999	2.015	2.031	2.048	2.064	2.080	2.097	2.114	2.130	2.147
-9	2.885	2.908	2.931	2.954	2.978	3.001	3.025	3.049	3.073	3.097	-9	2.164	2.181	2.199	2.216	2.234	2.251	2.269	2.287	2.305	2.323
-8	3.121	3.146	3.171	3.196	3.221	3.246	3.271	3.297	3.323	3.348	-8	2.341	2.360	2.378	2.397	2.416	2.435	2.454	2.473	2.492	2.511
-7	3.375	3.401	3.427	3.454	3.481	3.508	3.535	3.562	3.590	3.618	-7	2.531	2.551	2.571	2.591	2.611	2.631	2.651	2.672	2.693	2.714
-6	3.646	3.674	3.702	3.731	3.759	3.788	3.818	3.847	3.876	3.906	-6	2.734	2.756	2.777	2.798	2.820	2.842	2.863	2.885	2.908	2.930
-5	3.936	3.966	3.997	4.027	4.058	4.089	4.120	4.151	4.183	4.215	-5	2.952	2.975	2.998	3.021	3.044	3.067	3.090	3.114	3.138	3.161
-4	4.247	4.279	4.312	4.344	4.377	4.410	4.444	4.477	4.511	4.545	-4	3.185	3.210	3.234	3.259	3.283	3.308	3.333	3.358	3.384	3.409
-3	4.579	4.614	4.649	4.684	4.719	4.754	4.790	4.826	4.862	4.898	-3	3.435	3.461	3.487	3.513	3.539	3.566	3.593	3.620	3.647	3.674
-2	4.935	4.972	5.009	5.046	5.084	5.121	5.159	5.198	5.236	5.275	-2	3.701	3.729	3.757	3.785	3.813	3.841	3.870	3.899	3.928	3.957
-1	5.314	5.354	5.393	5.433	5.473	5.514	5.554	5.595	5.637	5.678	-1	3.986	4.016	4.045	4.075	4.105	4.136	4.166	4.197	4.228	4.258
0	5.720	5.762	5.804	5.847	5.889	5.933	5.976	6.020	6.064	6.108	0	4.290	4.322	4.353	4.385	4.417	4.450	4.482	4.515	4.548	4.581

Vapour Pressure and Boiling Point of Water

°C	Saturation pressure in millibar ¹										Boiling point in degree Celsius*										
	0	1	2	3	4	5	6	7	8	9	mbar	0	1	2	3	4	5	6	7	8	9
0	6.11	6.15	6.20	6.24	6.29	6.33	6.38	6.43	6.47	6.52	0	-16.52	-12.90	-8.35	-5.02	-2.40	-0.21	+1.90	3.78	5.46	
1	6.57	6.61	6.66	6.71	6.76	6.81	6.86	6.90	6.95	7.00	10	6.99	8.38	10.67	12.90	15.00	17.00	18.90	20.70	22.40	
2	7.05	7.11	7.16	7.21	7.26	7.31	7.36	7.42	7.47	7.52	20	17.52	18.29	19.07	19.84	20.61	21.38	22.15	22.92	23.69	
3	7.58	7.63	7.68	7.74	7.79	7.85	7.90	7.96	8.02	8.07	30	24.10	24.65	25.20	25.75	26.30	26.85	27.40	27.95	28.50	
4	8.13	8.19	8.24	8.30	8.36	8.42	8.48	8.54	8.60	8.66	40	28.99	29.41	29.83	30.25	30.67	31.09	31.51	31.93	32.35	
5	8.72	8.78	8.84	8.90	8.97	9.03	9.09	9.15	9.22	9.28	50	32.90	33.26	33.61	33.96	34.31	34.66	35.01	35.36	35.71	
6	9.35	9.41	9.48	9.54	9.61	9.67	9.74	9.81	9.88	9.94	60	36.19	36.49	36.79	37.09	37.39	37.69	37.99	38.29	38.59	
7	10.01	10.08	10.15	10.22	10.29	10.36	10.43	10.51	10.58	10.65	70	39.03	39.29	39.54	39.79	40.04	40.29	40.54	40.79	41.04	
8	10.72	10.80	10.87	10.94	11.02	11.09	11.17	11.24	11.32	11.40	80	41.54	41.77	41.99	42.21	42.43	42.65	42.87	43.09	43.31	
9	11.47	11.55	11.63	11.71	11.79	11.87	11.95	12.03	12.11	12.19	90	43.79	44.00	44.21	44.42	44.63	44.84	45.05	45.26	45.47	
10	12.27	12.36	12.44	12.52	12.61	12.69	12.78	12.86	12.95	13.03	100	45.84	46.03	46.23	46.42	46.61	46.80	46.99	47.17	47.35	
11	13.12	13.21	13.30	13.38	13.47	13.56	13.65	13.74	13.83	13.93	110	47.72	47.89	48.06	48.23	48.40	48.57	48.74	48.91	49.08	
12	14.02	14.11	14.20	14.30	14.39	14.49	14.58	14.68	14.77	14.87	120	49.45	49.62	49.79	49.96	50.13	50.29	50.46	50.63	50.79	
13	14.97	15.07	15.17	15.27	15.37	15.47	15.57	15.67	15.77	15.87	130	51.07	51.22	51.37	51.52	51.67	51.82	51.97	52.12	52.27	
14	15.98	16.08	16.19	16.29	16.40	16.50	16.61	16.72	16.83	16.94	140	52.58	52.72	52.86	53.00	53.14	53.28	53.42	53.56	53.70	
15	17.04	17.15	17.26	17.37	17.49	17.60	17.71	17.83	17.94	18.06	150	54.00	54.14	54.28	54.41	54.55	54.68	54.82	54.95	55.08	
16	18.17	18.29	18.41	18.52	18.64	18.76	18.88	19.00	19.12	19.25	160	55.35	55.48	55.61	55.74	55.87	56.00	56.13	56.26	56.39	
17	19.37	19.49	19.61	19.74	19.86	19.99	20.12	20.24	20.37	20.50	170	56.62	56.74	56.87	56.99	57.11	57.23	57.35	57.47	57.59	
18	20.63	20.76	20.89	21.02	21.16	21.29	21.42	21.56	21.69	21.83	180	57.93	57.98	58.11	58.23	58.35	58.47	58.59	58.71	58.83	
19	21.96	22.10	22.24	22.38	22.52	22.66	22.80	22.94	23.09	23.23	190	58.99	59.10	59.21	59.32	59.43	59.54	59.65	59.76	59.87	
20	23.37	23.52	23.66	23.81	23.96	24.11	24.26	24.41	24.56	24.71	200	60.09	60.20	60.31	60.42	60.53	60.64	60.75	60.86	60.97	
21	24.86	25.01	25.17	25.32	25.48	25.64	25.79	25.95	26.11	26.27	210	61.15	61.25	61.35	61.45	61.55	61.65	61.75	61.85	61.95	
22	26.43	26.59	26.75	26.92	27.08	27.25	27.41	27.58	27.75	27.92	220	62.17	62.26	62.36	62.46	62.56	62.66	62.76	62.86	62.96	
23	28.09	28.26	28.43	28.60	28.77	28.95	29.12	29.30	29.48	29.65	230	63.14	63.24	63.34	63.44	63.54	63.64	63.74	63.84	63.94	
24	29.83	30.01	30.19	30.37	30.56	30.74	30.92	31.11	31.30	31.48	240	64.09	64.18	64.28	64.38	64.48	64.58	64.68	64.78	64.88	
25	31.67	31.86	32.05	32.24	32.43	32.63	32.82	33.02	33.21	33.41	250	64.99	65.08	65.18	65.28	65.38	65.48	65.58	65.68	65.78	
26	33.61	33.81	34.01	34.21	34.41	34.62	34.82	35.03	35.23	35.44	260	65.87	65.96	66.06	66.16	66.26	66.36	66.46	66.56	66.66	
27	35.65	35.86	36.07	36.28	36.50	36.71	36.92	37.14	37.36	37.58	270	66.72	66.81	66.91	67.01	67.11	67.21	67.31	67.41	67.51	
28	37.80	38.02	38.24	38.46	38.69	38.91	39.14	39.37	39.59	39.82	280	67.55	67.63	67.73	67.83	67.93	68.03	68.13	68.23	68.33	
29	40.06	40.29	40.52	40.76	40.99	41.23	41.47	41.71	41.95	42.19	290	68.35	68.43	68.53	68.63	68.73	68.83	68.93	69.03	69.13	
30	42.43	42.67	42.92	43.17	43.41	43.66	43.91	44.17	44.42	44.67	300	69.13	69.20	69.30	69.40	69.50	69.60	69.70	69.80	69.90	
31	44.93	45.18	45.44	45.70	45.96	46.22	46.49	46.75	47.02	47.28	310	69.88	69.96	70.06	70.16	70.26	70.36	70.46	70.56	70.66	
32	47.55	47.82	48.09	48.36	48.64	48.91	49.19	49.47	49.75	50.03	320	70.62	70.69	70.79	70.89	70.99	71.09	71.19	71.29	71.39	
33	50.31	50.59	50.87	51.16	51.45	51.74	52.03	52.32	52.61	52.90	330	71.33	71.40	71.50	71.60	71.70	71.80	71.90	72.00	72.10	
34	53.20	53.50	53.80	54.10	54.40	54.70	55.00	55.31	55.62	55.93	340	72.03	72.10	72.20	72.30	72.40	72.50	72.60	72.70	72.80	
35	56.24	56.55	56.86	57.18	57.49	57.81	58.13	58.45	58.77	59.10	350	72.71	72.78	72.88	72.98	73.08	73.18	73.28	73.38	73.48	
36	59.42	59.75	60.08	60.41	60.74	61.07	61.41	61.74	62.08	62.42	360	73.38	73.44	73.54	73.64	73.74	73.84	73.94	74.04	74.14	
37	62.76	63.11	63.45	63.80	64.14	64.49	64.84	65.20	65.55	65.91	370	74.02	74.09	74.19	74.29	74.39	74.49	74.59	74.69	74.79	
38	66.26	66.62	66.99	67.35	67.71	68.08	68.45	68.82	69.19	69.56	380	74.66	74.72	74.82	74.92	75.02	75.12	75.22	75.32	75.42	
39	69.93	70.31	70.69	71.07	71.45	71.83	72.22	72.61	72.99	73.39	390	75.28	75.34	75.44	75.54	75.64	75.74	75.84	75.94	76.04	
40	73.78	74.17	74.57	74.97	75.37	75.77	76.17	76.58	76.98	77.39	400	75.89	75.95	76.05	76.15	76.25	76.35	76.45	76.55	76.65	
41	77.80	78.22	78.63	79.05	79.47	79.89	80.31	80.73	81.16	81.59	410	76.48	76.54	76.64	76.74	76.84	76.94	77.04	77.14	77.24	
42	82.02	82.45	82.88	83.32	83.75	84.19	84.64	85.08	85.53	85.97	420	77.06	77.12	77.22	77.32	77.42	77.52	77.62	77.72	77.82	
43	86.42	86.88	87.33	87.79	88.24	88.70	89.17	89.63	90.10	90.56	430	77.63	77.69	77.79	77.89	77.99	78.09	78.19	78.29	78.39	
44	91.03	91.51	91.98	92.46	92.94	93.42	93.90	94.39	94.87	95.36	440	78.19	78.25	78.35	78.45	78.55	78.65	78.75	78.85	78.95	
45	95.86	96.35	96.85	97.34	97.84	98.35	98.85	99.36	99.87	100.38	450	78.74	78.80	78.90	79.00	79.10	79.20	79.30	79.40	79.50	
46	100.89	101.41	101.93	102.45	102.97	103.50	104.03	104.56	105.09	105.62	460	79.28	79.34	79.44	79.54	79.64	79.74	79.84	79.94	80.04	
47	106.16	106.70	107.24	107.78	108.33	108.88	109.43	109.98	110.54	111.10	470	79.81	79.86	79.96	80.06	80.16	80.26	80.36	80.46	80.56	
48	111.66	112.22	112.79	113.36	113.93	114.50	115.07	115.65	116.23	116.81	480	80.33	80.38	80.48	80.58	80.68	80.78	80.88	80.98	81.08	
49	117.40	117.99	118.58	119.17	119.77	120.37	120.97	121.57	122.18	122.79	490	80.84	80.89	80.99	81.09	81.19	81.29	81.39	81.49	81.59	
50	123.40	124.01	124.63	125.25	125.87	126.49	127.12	127.75	128.38	129.01	500	81.35	81.40	81.50	81.60	81.70	81.80	81.90	82.00	82.10	
51	129.65	130.29	130.93	131.58	132.23	132.88	133.53	134.19	134.84	135.51	510	81.84	81.89	81.99	82.09	82.19	82.29	82.39	82.49	82.59	
52	136.17	136.84	137.51	138.18	138.86	139.54	140.22	140.91	141.60	142.29	520	82.33	82.37	82.47	82.57	82.67	82.77	82.87	82.97	83.07	
53	142.98	143.68	144.38	145.08	145.78	146.49	147.20	147.91	148.63	149.35	530	82.80	82.85	82.95	83.05	83.15	83.25	83.35	83.45	83.55	
54	150.07	150.80	151.53	152.26	152.99	153.73	154.47	155.21	155.96	156.71	540	83.27	83.32	83.42	83.52	83.62	83.72	83.82	83.92	84.02	
55	157.46	158.22	159.00	159.76	160.50	161.27	162.04	162.82	163.59	164.38	550	83.74	83.78	83.88	83.98						

Reduction of Saturated Gas Volumes to Body Temperature (37°C) for 490–780 mm Hg* 259

a table gives factors for conversion of spirometer
to lung values calculated from the formula

is here

p = measured pressure of the spirometer volume (mm Hg)

t = measured temperature of the pycnometer volume ($^{\circ}\text{C}$)

P_{H_2O} and $P_{H_2O}^{37}$ = pressure of water vapour at the measured temperature of the spirometric volume and at 37 °C in the lungs respectively

 α = volume coefficient of expansion of air per °C (see page 260)

$$\frac{(p - p_{\text{H}_2\text{O}})(1 + 37\alpha)}{(p - p_{\text{H}_2\text{O}})(1 + 4\alpha)}$$

$$(\rho - \rho_{\text{ext}}) (1 + f \alpha)$$

[illegible]

10. *Journal of the American Statistical Association*, 1997, 92, 1003-1010.

	490	500	510	520	530	540	550	560	570	580	590	600	610	620	630
0	12447	12423	12400	12378	12357	12337	12317	12299	12281	12263	12247	12231	12215	12200	12186
1	2393	2369	2347	2325	2304	2284	2265	2246	2228	2211	2195	2179	2164	2149	2134
2	2339	2315	2293	2271	2250	2231	2212	2193	2176	2159	2143	2127	2112	2097	2083
3	2284	2261	2239	2217	2197	2177	2159	2141	2123	2107	2091	2075	2060	2046	2032
4	2229	2206	2184	2163	2143	2124	2105	2088	2071	2054	2038	2023	2008	1994	1980
5	12174	12151	12130	12109	12089	12070	12052	12034	12018	12001	11986	11971	11956	11942	11927
6	2118	2096	2075	2054	2035	2016	1998	1981	1964	1948	1933	1918	1904	1890	1877
7	2062	2041	2020	2000	1980	1962	1944	1927	1911	1895	1880	1866	1852	1838	1825
8	2006	1985	1964	1944	1926	1907	1890	1873	1857	1842	1827	1813	1799	1786	1773
9	1949	1928	1908	1889	1870	1853	1836	1819	1803	1788	1774	1760	1746	1733	1720
10	11892	11872	11852	11833	11813	11792	11771	11754	11749	11734	11720	11706	11693	11680	11666
11	1835	1814	1795	1776	1759	1743	1727	1709	1694	1680	1666	1652	1639	1627	1614
12	1777	1757	1738	1720	1702	1685	1669	1654	1639	1625	1611	1598	1585	1573	1561
13	1718	1698	1680	1662	1645	1629	1613	1598	1584	1570	1556	1543	1531	1519	1507
14	1658	1640	1622	1604	1588	1572	1556	1542	1528	1514	1501	1488	1476	1464	1453
15	1598	1580	1562	1544	1529	1514	1499	1485	1471	1458	1445	1433	1421	1409	1398
16	1538	1520	1503	1486	1471	1456	1441	1427	1414	1401	1389	1377	1365	1354	1343
17	1476	1459	1442	1426	1411	1397	1383	1369	1356	1344	1332	1320	1309	1298	1288
18	1414	1397	1381	1366	1351	1337	1323	1310	1298	1286	1274	1263	1252	1242	1232
19	1351	1335	1319	1304	1290	1276	1263	1251	1239	1227	1216	1205	1195	1184	1175
20	1287	1271	1256	1242	1228	1215	1203	1191	1179	1168	1157	1146	1136	1127	1117
21	1221	1207	1193	1179	1166	1153	1141	1129	1118	1108	1097	1087	1078	1068	1059
22	1156	1141	1128	1115	1102	1090	1079	1068	1057	1047	1037	1027	1018	1009	1001
23	1092	1075	1062	1050	1038	1026	1015	1005	995	985	975	966	958	949	941
24	1020	1003	990	978	967	957	947	937	928	919	910	903	896	888	881
25	10951	10932	10913	10894	10876	10858	10841	10824	10807	10791	10776	10761	10746	10731	10716
26	0880	0860	0843	0826	0810	0794	0779	0764	0749	0734	0719	0704	0689	0674	0659
27	0608	0589	0571	0554	0537	0521	0505	0489	0474	0459	0444	0429	0414	0399	0384
28	0333	0315	0298	0281	0265	0249	0233	0218	0203	0188	0173	0158	0143	0128	0113
29	0060	0043	0026	0010	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
30	10384	10376	10368	10361	10354	10348	10342	10336	10330	10324	10319	10314	10309	10304	10299
31	0506	0499	0492	0486	0480	0474	0469	0464	0459	0454	0449	0444	0440	0436	0432
32	0426	0420	0413	0407	0401	0395	0390	0386	0383	0378	0374	0369	0365	0362	0358
33	0345	0340	0335	0331	0327	0323	0319	0315	0312	0309	0305	0302	0299	0296	0293
34	0361	0358	0354	0351	0348	0345	0342	0339	0336	0334	0331	0329	0327	0324	0322
35	10176	10174	10171	10169	10167	10165	10163	10161	10159	10157	10156	10154	10153	10151	10150
36	0089	0088	0087	0086	0084	0083	0082	0081	0081	0080	0079	0078	0077	0076	0075
	640	650	660	670	680	690	700	710	720	730	740	750	760	770	780
0	12172	12158	12145	12133	12120	12109	12097	12086	12075	12065	12054	12045	12033	12025	12016
1	2121	2107	2094	2082	2070	2058	2047	2036	2025	2015	2005	1995	1983	1976	1968
2	2070	2056	2044	2031	2019	2008	1997	1986	1975	1965	1955	1945	1936	1927	1918
3	2018	2005	1993	1981	1969	1957	1946	1936	1925	1915	1903	1896	1886	1877	1869
4	1967	1954	1942	1930	1918	1907	1896	1883	1873	1865	1855	1846	1837	1828	1819
5	11916	11903	11891	11879	11867	11856	11846	11835	11825	11815	11806	11796	11787	11778	11770
6	1864	1852	1840	1828	1817	1806	1795	1785	1775	1765	1756	1746	1738	1729	1721
7	1812	1800	1788	1777	1765	1753	1744	1734	1724	1713	1706	1697	1688	1679	1671
8	1760	1746	1736	1725	1714	1704	1693	1683	1674	1664	1655	1647	1638	1629	1621
9	1708	1696	1685	1674	1663	1652	1642	1633	1623	1614	1605	1596	1588	1580	1572
10	11655	11644	11633	11622	11611	11601	11591	11582	11572	11563	11554	11546	11538	11530	11522
11	1603	1591	1580	1570	1559	1549	1540	1530	1521	1512	1504	1495	1487	1479	1472
12	1549	1538	1528	1517	1507	1497	1488	1479	1470	1461	1453	1444	1437	1429	1421
13	1496	1485	1475	1464	1455	1445	1436	1427	1418	1410	1401	1393	1386	1378	1371
14	1442	1431	1421	1411	1402	1392	1383	1375	1366	1358	1350	1342	1334	1327	1320
15	1388	1377	1367	1358	1348	1339	1331	1322	1314	1306	1298	1290	1283	1276	1269
16	1333	1323	1313	1304	1295	1286	1277	1268	1260	1252	1246	1238	1231	1224	1217
17	1278	1268	1258	1249	1241	1232	1224	1216	1208	1200	1193	1186	1179	1172	1166
18	1222	1212	1203	1194	1186	1178	1170	1162	1154	1147	1140	1133	1126	1120	1113
19	1165	1156	1147	1139	1131	1123	1115	1108	1101	1093	1086	1080	1073	1067	1060
20	11108	11100	11091	11083	11075	11067	11060	11053	11046	11039	11032	11026	11020	11014	11008
21	1058	1042	1034	1026	1019	1011	1004	997	991	984	978	972	966	960	955
22	0992	0984	0976	0969	0962	0955	0948	0941	0935	0929	0923	0917	0911	0905	0900
23	0933	0926	0918	0911	0904	0897	0891	0885	0879	0873	0867	0861	0856	0851	0846
24	0873	0866	0859	0852	0846	0840	0833	0827	0822	0816	0810	0805	0800	0795	0790
25	10812	10806	10799	10793	10787	10781	10775	10769	10763	10757	10751	10745	10740	10734	10729
26	0751	0744	0738	0732	0727	0721	0716	0710	0705	0700	0695	0691	0686	0682	0677
27	0688	0682	0677	0671	0666	0661	0656	0651	0646	0642	0637	0633	0629	0625	0621
28	0625	0619	0614	0609	0604	0599	0595	0590	0586	0582	0578	0574	0570	0566	0562
29	0560	0555	0551	0546	0542	0537	0533	0529	0525	0521	0518	0514	0511	0507	0503
30	10495	10490	10486	10482	10478	10474	10470	10467	10463	10460	10457	10453	10450	10447	10444
31	0428	0424	0420	0417	0413	0410	0407	0403	0400	0397	0395	0392	0389	0386	0383
32	0360	0357	0353	0350	0347	0345	0342	0339	0337	0334	0332	0329	0327	0325	0323
33	0291	0288	0285	0283	0280	0278	0276	0274	0272	0270	0268	0266	0264	0262	0260
34	0220	0218	0216	0214	0212	0211	0209	0207	0206	0204	0203	0201	0199	0198	0197
35	0148	0147	0144	0144	0143	0143	0143	0143	0143	0143	0143	0143	0143	0143	0143
36	0075	0074	0073	0073	0073	0072	0072	0071	0070	0070	0070	0070	0068	0067	0066

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The following remarks are applicable to any other gas in place of air without appreciable error (see under 'Basis of calculation', below).

Explanation of the tables

mm Hg; Values in the uppermost line of each table = observed pressure in mm Hg of the measured gas volume. Under many conditions of measurement this will be the same as the ambient (atmospheric) pressure, i.e., the observed barometric pressure after correction for temperature. Correction for pressure of water vapour under conditions of saturation is also provided for in the table (see under "sat." below).

°C. Values in the extreme left-hand column = observed temperature of the measured gas volume.

dry Factor for the reduction of the measured volume of dry gas to *normal conditions* (0°C, 760 mm Hg, dry). Normal gas volumes are indicated by the abbreviation NTP (normal temperature and pressure). American lung specialists have introduced the abbreviation STPD (standard lung temperature and pressure, dry).

sal. Factor for the reduction of the measured volume of gas *saturated with water vapour* to normal conditions (0°C, 760 mm Hg, dry). Gases may be assumed to be saturated with water vapour if they are in contact with water. This applies to the air in the lungs and to exhaled air, as also to spirometer air (if not dried). For the pressure of saturated water vapour at various temperatures see pages 256–258.

Use of the tables

A. Reduction of measured gas volumes to normal conditions (NTP)

The measured volume is multiplied by the factor appropriate to the conditions of measurement (temperature, pressure, dry or saturated).

Example: 1. What is the volume at NTP of 1.6 l of dry gas measured at 25°C and 712 mm Hg? Required volume at NTP = $1.6 \times 0.8581 = 1.3730$ l (NTP).

2. What is the volume at NTP of 1.6 l of gas saturated with water vapour and measured at 25 °C and 712 mm Hg? Required volume at NTP = $1.6 \times 0.8295 = 1.3272$ l (NTP). This is the type of calculation required to convert spirometer values to NTP.

B. Conversion of measured volumes to other conditions

The measured volume is multiplied by the appropriate conversion factor NTP and the resulting value divided by the conversion factor corresponds to the required conditions (temperature, pressure, dry or moist).

Examples: 1. What will be the volume occupied by 1.6 l of gas measured at 25°C and 730 mm Hg in contact with water when warmed at constant pressure to 37°C? Required volume = $1.6 \times 0.8512/0.7912 = 1.7213$ l. The type of calculation required to convert spirometer values to lung values is called BTPS (body temperature and pressure, saturated) and is frequently used to indicate gas volumes under lung conditions, i.e., 37°C, atmospheric pressure, saturated with water vapour. For direct conversion factors for spirometer to lung values see page 259.

2. What will be the volume occupied by 1.6 l of dry gas measured at 0°C, 600 mm Hg after saturation with water vapor, warming to 25°C and compression to 760 mm Hg? Required volume = $1.6 \times 0.7895/0.8873 = 1.423$ l

Basis of calculation

The conversion factors have been calculated on the basis of the following formulae:

$$\begin{aligned} \text{Conversion factor for reduction of dry gas volumes to normal} &= \frac{p}{760(1 + \alpha t)}, & \text{Conversion factor for reduction of saturated gas volumes to normal} &= \frac{p - p_{H_2O}}{760(1 + \alpha t)}, \text{ where:} \end{aligned}$$

p, t pressure in mm Hg and temperature in $^{\circ}\text{C}$ of the measured gas volume

p_{H_2O} pressure of saturated water vapour at the temperature t (see page 256-258).

α volume coefficient of thermal expansion of the gas between 0 and 100° C at a constant pressure of 760 mm Hg. In these tables the value for air is 0.003670 per °C (REGNAULT, 1842), has been used. Under the same conditions the value for an ideal gas is 0.003661 (= 1/273.15), for nitrogen 0.003671, for carbon monoxide 0.003669, for carbon dioxide 0.003723 for acetylene 0.003739. The conversion factors are therefore closely applicable without sensible error to other gases in addition to air.

Note that in calculating the factors the 4th decimal place has been obtained by rounding off upwards or downwards. Any discrepancies with factors given in other tables (e.g., in the *Handbook of Chemistry and Physics*) are due to the use of other values for the expansion coefficient or conversion factors.

mm Hg 600			601		602		603		604		605		606		607		608		609	
°C	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.
0	0.7895	0.7834	0.7908	0.7848	0.7921	0.7861	0.7934	0.7874	0.7947	0.7887	0.7961	0.7900	0.7974	0.7913	0.7987	0.7927	0.8000	0.7940	0.8013	0.7953
1	7866	7801	7879	7814	7892	7828	7905	7841	7918	7854	7931	7867	7945	7880	7958	7893	7971	7906	7984	7919
2	7837	7768	7850	7781	7863	7794	7876	7807	7889	7820	7903	7833	7916	7846	7929	7859	7942	7873	7955	7885
3	7809	7735	7822	7748	7835	7761	7848	7774	7861	7787	7874	7800	7887	7813	7900	7826	7913	7839	7926	7852
4	7781	7701	7793	7714	7806	7727	7819	7740	7832	7753	7845	7766	7858	7779	7871	7792	7884	7805	7897	7818
5	0.7752	0.7668	0.7765	0.7681	0.7778	0.7694	0.7791	0.7707	0.7804	0.7720	0.7817	0.7733	0.7830	0.7745	0.7843	0.7758	0.7856	0.7771	0.7869	0.7784
6	7725	7634	7738	7647	7750	7660	7763	7673	7776	7686	7789	7699	7802	7712	7815	7724	7823	7737	7841	7750
7	7697	7601	7710	7613	7723	7626	7735	7639	7748	7652	7761	7665	7774	7678	7787	7690	7800	7703	7812	7720
8	7670	7567	7682	7580	7695	7592	7708	7605	7721	7618	7733	7631	7746	7643	7759	7656	7772	7669	7785	7702
9	7642	7533	7655	7545	7668	7558	7681	7571	7693	7584	7706	7596	7719	7609	7731	7622	7744	7635	7757	7642
10	0.7615	0.7498	0.7628	0.7511	0.7641	0.7524	0.7653	0.7536	0.7666	0.7549	0.7679	0.7562	0.7691	0.7575	0.7704	0.7587	0.7717	0.7600	0.7729	0.7613
11	7588	7464	7601	7477	7614	7489	7626	7502	7639	7514	7652	7527	7664	7540	7677	7552	7690	7565	7702	7578
12	7562	7429	7574	7442	7587	7454	7600	7467	7612	7480	7625	7492	7637	7505	7650	7517	7663	7530	7675	7543
13	7535	7394	7548	7407	7560	7419	7573	7432	7585	7444	7598	7457	7611	7470	7623	7482	7636	7495	7648	7507
14	7509	7359	7521	7371	7534	7384	7546	7396	7559	7409	7572	7421	7584	7434	7597	7447	7609	7459	7622	7470
15	0.7483	0.7323	0.7495	0.7336	0.7508	0.7348	0.7520	0.7361	0.7533	0.7373	0.7545	0.7386	0.7558	0.7398	0.7570	0.7411	0.7583	0.7423	0.7595	0.7435
16	7457	7287	7469	7300	7482	7312	7494	7325	7507	7337	7519	7350	7531	7362	7544	7374	7556	7387	7569	7399
17	7431	7251	7443	7264	7456	7276	7468	7288	7481	7301	7493	7313	7505	7325	7518	7338	7530	7350	7543	7362
18	7406	7215	7418	7227	7430	7239	7443	7252	7455	7264	7467	7276	7480	7289	7492	7301	7504	7313	7517	7329

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Reduction of Gas Volumes

mm Hg	630	631	632	633	634	635	636	637	638	639
°C	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.
0	0.8269	0.8229	0.8303	0.8242	0.8316	0.8256	0.8329	0.8269	0.8342	0.8282
1	8259	8195	8272	8208	8285	8221	8298	8234	8312	8247
2	8229	8160	8242	8173	8255	8186	8268	8199	8281	8212
3	8199	8125	8212	8138	8225	8151	8238	8164	8251	8177
4	8170	8090	8183	8103	8195	8116	8208	8129	8221	8142
5	0.8140	0.8056	0.8153	0.8068	0.8166	0.8081	0.8179	0.8091	0.8192	0.8107
6	8111	8021	8124	8033	8137	8046	8149	8059	8162	8072
7	8082	7985	8095	7998	8108	8011	8120	8024	8133	8037
8	8053	7950	8066	7963	8079	7976	8091	7989	8104	8001
9	8024	7915	8037	7928	8050	7940	8063	7953	8075	7966
10	0.7996	0.7879	0.8009	0.7892	0.8021	0.7905	0.8034	0.7917	0.8047	0.7930
11	7968	7843	7980	7856	7993	7869	8006	7881	8018	7894
12	7940	7807	7952	7820	7965	7832	7978	7845	7990	7858
13	7912	7771	7925	7784	7937	7796	7950	7809	7962	7821
14	7884	7734	7897	7747	7909	7759	7922	7772	7934	7784
15	0.7857	0.7697	0.7869	0.7710	0.7882	0.7722	0.7894	0.7735	0.7907	0.7747
16	7830	7660	7842	7673	7855	7685	7867	7698	7879	7710
17	7803	7623	7815	7635	7827	7647	7840	7660	7852	7672
18	7776	7585	7788	7597	7800	7609	7813	7622	7825	7634
19	7749	7546	7761	7559	7774	7571	7786	7583	7798	7596
20	0.7723	0.7508	0.7735	0.7520	0.7747	0.7532	0.7759	0.7544	0.7772	0.7557
21	7696	7468	7709	7481	7721	7493	7733	7505	7745	7517
22	7670	7429	7682	7441	7695	7453	7707	7465	7719	7477
23	7644	7389	7656	7401	7668	7413	7681	7425	7693	7437
24	7618	7348	7631	7360	7643	7372	7655	7384	7667	7396
25	0.7593	0.7307	0.7605	0.7319	0.7617	0.7331	0.7629	0.7343	0.7641	0.7355
26	7567	7265	7579	7277	7591	7289	7603	7301	7615	7313
27	7542	7222	7554	7234	7566	7246	7578	7258	7590	7270
28	7517	7179	7529	7191	7541	7203	7553	7215	7565	7226
29	7492	7135	7504	7147	7516	7159	7528	7170	7540	7182
30	0.7467	0.7090	0.7479	0.7102	0.7491	0.7114	0.7503	0.7126	0.7515	0.7138
31	7443	7045	7455	7056	7466	7068	7478	7080	7490	7092
32	7418	6998	7430	7010	7442	7022	7454	7034	7465	7045
33	7394	6951	7406	6963	7417	6975	7429	6986	7441	6998
34	7370	6903	7382	6915	7393	6927	7405	6938	7417	6950
35	0.7346	0.6854	0.7358	0.6866	0.7369	0.6877	0.7381	0.6889	0.7393	0.6901
36	7322	6804	7334	6816	7345	6827	7357	6839	7369	6851
37	7298	6753	7310	6765	7322	6776	7333	6788	7345	6799
38	7275	6701	7286	6713	7298	6724	7310	6736	7321	6747
39	7252	6648	7263	6659	7275	6671	7286	6682	7298	6694
40	0.7228	0.6594	0.7240	0.6605	0.7251	0.6617	0.7263	0.6628	0.7274	0.6639
41	7205	6538	7217	6549	7228	6561	7240	6572	7251	6584
42	7182	6481	7194	6493	7205	6504	7217	6515	7228	6527
43	0.8421	0.8361	0.8434	0.8374	0.8447	0.8387	0.8461	0.8400	0.8474	0.8413
44	8390	8326	8403	8339	8416	8352	8430	8365	8443	8378
45	8360	8291	8373	8304	8386	8317	8399	8330	8412	8343
46	8329	8255	8342	8268	8355	8281	8368	8294	8381	8307
47	8299	8220	8312	8233	8325	8246	8338	8259	8351	8272
48	0.8269	0.8185	0.8282	0.8198	0.8295	0.8211	0.8308	0.8224	0.8321	0.8236
49	8240	8149	8252	8162	8265	8175	8278	8188	8291	8201
50	8210	8114	8223	8127	8236	8139	8249	8152	8261	8165
51	8181	8078	8194	8091	8206	8104	8219	8116	8232	8129
52	8152	8042	8165	8055	8177	8068	8190	8080	8203	8093
53	0.8123	0.8006	0.8136	0.8019	0.8148	0.8031	0.8161	0.8044	0.8174	0.8057
54	8094	7970	8107	7982	8120	7995	8132	8008	8145	8020
55	8066	7933	8078	7946	8091	7958	8104	7971	8116	7984
56	8038	7897	8050	7909	8063	7922	8075	7934	8088	7947
57	8010	7860	8022	7872	8035	7885	8047	7897	8060	7910
58	0.7982	0.7822	0.7994	0.7835	0.8007	0.7847	0.8019	0.7860	0.8032	0.7872
59	7954	7785	7966	7797	7979	7809	7991	7822	8004	7834
60	7927	7747	7939	7759	7951	7771	7964	7784	7976	7796
61	7899	7708	7912	7721	7924	7733	7936	7745	7949	7758
62	7872	7669	7884	7682	7897	7694	7909	7706	7921	7719
63	0.7845	0.7630	0.7857	0.7643	0.7870	0.7655	0.7882	0.7667	0.7894	0.7679
64	7818	7591	7831	7603	7843	7615	7855	7587	7867	7640
65	7792	7551	7804	7563	7816	7575	7828	7587	7841	7599
66	7766	7510	7778	7522	7790	7534	7802	7546	7814	7558
67	7739	7469	7751	7481	7764	7493	7776	7505	7788	7517
68	0.7713	0.7427	0.7725	0.7439	0.7737	0.7451	0.7750	0.7463	0.7762	0.7475
69	7688	7385	7700	7397	7712	7409	7724	7421	7736	7433
70	7662	7342	7674	7354	7686	7366	7698	7378	7710	7390
71	7636	7298	7648	7310	7660	7322	7672	7334	7684	7346
72	7611	7254	7623	7266	7635	7278	7647	7289	7659	7301
73	0.7686	0.7209	0.7698	0.7220	0.7710	0.7232	0.7722	0.7244	0.7734	0.7256
74	7651	7163	7663	7175	7674	7186	7686	7198	7698	7210
75	7625	7116	7637	7128	7649	7140	7661	7151	7673	7163
76	7599	7069	7611	7080	7623	7092	7635	7104	7647	7116
77	7573	7020	7585	7032	7597	7044	7609	7055	7621	7067
78	0.7659	0.7071	0.7671	0.7083	0.7683	0.7095	0.7695	0.7107	0.7707	0.7119
79	7624	6973	7636	6985	7648	6996	7660	7007	7672	7019
80	7598	6926	7610	6937	7622	6888	7634	6899	7646	6911
81	7572	6879	7584	6889	7596	6840	7608	6851	7620	6863
82	7546	6832	7558	6842	7570	6793	7582	6804	7594	6775
83	0.7632	0.6971	0.7644	0.6982	0.7656	0.6994	0.7668	0.7006	0.7680	0.7017
84	7511	6785	7523	6796	7535	6807	7547	6819	7559	6831
85	7485	6738	7497	6749	7509	6761	7521	6773	7533	6785
86	7459	6691	7471	6702	7483	6654	7495	6666	7507	6678
87	7433	6644	7445	6655	7457	6607	7469	6619	7481	6631
88	7407	6597	7419	6608	7431	6560	7443	6572	7455	6584
89	7381	6550	7393	6561	7407	6513	7419	6525	7431	6537
90	0.7607	0.6708	0.7619	0.6720	0.7631	0.6731	0.7643	0.6743	0.7655	0.6755
91	7355	6503	7367	6514	7379	6525	7391	6537	7403	6549
92	7329	6456	7341	6467	7353	6478	7365	6489	7377	6501
93	7303	6409	7315	6420	7327	6431	7339	6443	7351	6455
94	7277	6362	7289	6373	7301	6384	7313	6396	7325	6408
95	7251	6315	7263	6326	7275	6278	7287	6290	7299	6302
96	7225	6268	7237	6279	7249	6231	7261	6243	7273	6255
97	7199	6221	7211	6232	7223	6184	7235	6196	7247	6208
98	7173	6174	7185	6185	7197	6137	7209	6149	7221	6161
99	7147	6127	7159	6138	7171	6090	7183	6102	7195	6054
100	7121	6080	7133	6091	7145	6043	7157	6055	7169	6007

Reduction of Gas Volumes

mm Hg	670		671		672		673		674		675		676		677		678		679	
"C	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.
0	0.8816	0.8756	0.8829	0.8769	0.8842	0.8782	0.8855	0.8795	0.8868	0.8808	0.8882	0.8821	0.8895	0.8834	0.8908	0.8848	0.8921	0.8861	0.8934	0.8874
1	8784	8719	8797	8732	8810	8745	8823	8758	8836	8771	8849	8785	8862	8798	8875	8811	8888	8824	8902	8837
2	8752	8682	8765	8695	8778	8709	8791	8722	8804	8735	8817	8748	8830	8761	8843	8774	8856	8787	8869	8799
3	8720	8646	8733	8659	8746	8672	8759	8685	8772	8698	8785	8711	8798	8724	8811	8737	8824	8750	8837	8762
4	8688	8609	8701	8622	8714	8635	8727	8648	8740	8661	8753	8674	8766	8687	8779	8700	8792	8713	8805	8725
5	0.8657	0.8572	0.8670	0.8585	0.8683	0.8598	0.8696	0.8611	0.8709	0.8624	0.8722	0.8637	0.8734	0.8650	0.8747	0.8663	0.8760	0.8676	0.8773	0.8685
6	8626	8536	8639	8548	8652	8561	8664	8574	8677	8587	8690	8600	8703	8613	8716	8626	8729	8639	8742	8651
7	8595	8499	8608	8511	8621	8524	8633	8537	8646	8550	8659	8563	8672	8576	8685	8588	8698	8601	8710	8614
8	8564	8462	8577	8474	8590	8487	8603	8500	8615	8513	8628	8525	8641	8538	8654	8551	8667	8564	8679	8577
9	8534	8424	8547	8437	8559	8450	8572	8462	8585	8475	8598	8488	8610	8501	8623	8513	8636	8526	8649	8539
10	0.8504	0.8387	0.8516	0.8400	0.8529	0.8412	0.8542	0.8425	0.8554	0.8438	0.8567	0.8450	0.8580	0.8463	0.8593	0.8476	0.8605	0.8488	0.8618	0.8529
11	8474	8349	8486	8362	8499	8375	8512	8387	8524	8400	8537	8412	8550	8425	8562	8438	8575	8450	8588	8463
12	8444	8311	8457	8324	8469	8337	8482	8349	8494	8362	8507	8374	8520	8387	8532	8400	8545	8412	8557	8425
13	8414	8273	8427	8286	8439	8298	8452	8311	8465	8324	8477	8336	8490	8349	8502	8361	8515	8374	8527	8389
14	8385	8235	8397	8247	8410	8260	8423	8272	8435	8285	8448	8298	8460	8310	8473	8323	8485	8335	8498	8348
15	0.8356	0.8196	0.8368	0.8209	0.8381	0.8221	0.8393	0.8234	0.8406	0.8246	0.8418	0.8259	0.8431	0.8271	0.8443	0.8284	0.8456	0.8296	0.8468	0.8309
16	8327	8157	8339	8170	8352	8182	8364	8195	8377	8207	8389	8220	8401	8232	8414	8244	8426	8257	8439	8269
17	8298	8118	8310	8131	8323	8143	8335	8155	8348	8168	8360	8180	8372	8192	8385	8205	8397	8217	8410	8229
18	8270	8078	8282	8091	8294	8103	8307	8116	8319	8128	8331	8140	8344	8153	8356	8165	8368	8177	8381	8190
19	8241	8038	8253	8051	8266	8063	8278	8075	8290	8088	8303	8100	8315	8112	8327	8125	8340	8137	8352	8149
20	0.8213	0.7998	0.8225	0.8010	0.8237	0.8023	0.8250	0.8035	0.8262	0.8047	0.8274	0.8059	0.8287	0.8072	0.8299	0.8084	0.8311	0.8096	0.8323	0.8105
21	8185	7957	8197	7969	8209	7982	8222	7994	8234	8006	8246	8018	8258	8030	8270	8043	8283	8055	8295	8067
22	8157	7916	8169	7928	8182	7940	8194	7952	8206	7964	8218	7977	8230	7989	8242	8001	8255	8013	8267	8025
23	8130	7874	8142	7886	8154	7898	8166	7910	8178	7922	8190	7935	8202	7947	8215	7959	8227	7971	8239	7983
24	8102	7832	8114	7844	8126	7856	8138	7868	8151	7880	8163	7892	8175	7904	8187	7916	8199	7928	8211	7943
25	0.8075	0.7789	0.8087	0.7801	0.8099	0.7813	0.8111	0.7825	0.8123	0.7837	0.8135	0.7849	0.8147	0.7861	0.8159	0.7873	0.8171	0.7885	0.8183	0.7895
26	8048	7745	8060	7757	8072	7769	8084	7781	8096	7793	8108	7805	8120	7817	8132	7829	8144	7841	8156	7853
27	8021	7701	8033	7713	8045	7725	8057	7737	8069	7749	8081	7761	8093	7773	8105	7785	8117	7797	8129	7805
28	7994	7656	8006	7668	8018	7680	8030	7692	8042	7704	8054	7716	8066	7728	8078	7740	8090	7751	8102	7763
29	7968	7611	7980	7622	7992	7634	8003	7646	8015	7658	8027	7670	8039	7682	8051	7694	8063	7706	8075	7718
30	0.7941	0.7564	0.7953	0.7576	0.7965	0.7588	0.7977	0.7600	0.7989	0.7612	0.8001	0.7623	0.8013	0.7635	0.8024	0.7647	0.8036	0.7659	0.8048	0.7671
31	7915	7517	7927	7529	7939	7541	7951	7553	7963	7564	7974	7576	7986	7588	7998	7600	8010	7612	8022	7624
32	7889	7469	7901	7481	7913	7493	7925	7505	7936	7516	7948	7528	7960	7540	7972	7552	7983	7564	7995	7575
33	7863	7421	7875	7432	7887	7444	7899	7456	7910	7468	7922	7479	7934	7491	7946	7503	7957	7515	7969	7526
34	7838	7371	7849	7383	7861	7394	7873	7406	7885	7418	7896	7430	7908	7441	7920	7453	7931	7465	7943	7475
35	0.7812	0.7321	0.7824	0.7332	0.7836	0.7344	0.7847	0.7356	0.7859	0.7367	0.7871	0.7379	0.7882	0.7390	0.7894	0.7402	0.7906	0.7414	0.7917	0.7425
36	7787	7269	7799	7281	7810	7292	7822	7304	7833	7316	7845	7327	7857	7339	7868	7350	7880	7362	7892	7374
37	7762	7217	7773	7228	7785	7240	7797	7251	7808	7263	7820	7274	7831	7286	7843	7298	7854	7309	7866	7318
38	7737	7163	7748	7175	7760	7186	7771	7198	7783	7209	7795	7221	7806	7232	7818	7244	7829	7255	7841	7265
39	7712	7108	7723	7120	7735	7131	7747	7143	7758	7154	7770	7166	7781	7177	7793	7189	7804	7200	7816	7212
40	0.7687	0.7053	0.7699	0.7064	0.7710	0.7075	0.7722	0.7087	0.7733	0.7098	0.7745	0.7110	0.7756	0.7121	0.7768	0.7133	0.7779	0.7144	0.7791	0.7155
41	7663	6996	7674	7007	7686	7018	7697	7030	7709	7041	7720	7053	7731	7064	7743	7076	7754	7087	7766	7098
42	7638	6937	7650	6949	7661	6960	7673	6971	7684	6983	7695	6994	7707	7006	7718	7017	7730	7028	7741	7039

mm Hg	680		681		682		683		684		685		686		687		688		689	
"C	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.
0	0.8947	0.8887	0.8961	0.8900	0.8974	0.8913	0.8987	0.8927	0.9000	0.8940	0.9013	0.8953	0.9026	0.8966	0.9039	0.8979	0.9052	0.8992	0.9105	0.9018
1	8915	8850	8928	8863	8941	8876	8954	8889	8967	8903	8980	8916	8993	8929	9006	8942	9019	8955	9032	8968
2	8882	8813	8895	8832	8908	8839	8921	8852	8934	8865	8947	8878	8961	8884	8974	8894	8987	8905	8997	8918
3	8850	8776	8863	8789	8876	8802	8889	8815	8902	8828	8915	8841	8928	8851	8941	8867	8954	8878	8967	8889
4	8818	8739	8831	8752	8844	8765	8857	8778	8870	8791	8883	8804	8896	8817	8909	8830	8922	8843	8935	8855
5	0.8786	0.8702	0.8799	0.8715	0.8812	0.8727	0.8825	0.8740	0.8838	0.										

Reduction of Gas Volumes

mmHg	710		711		712		713		714		715		716		717		718		719	
	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.
0	0.9342	0.9282	0.9355	0.9295	0.9368	0.9308	0.9382	0.9321	0.9395	0.9334	0.9408	0.9348	0.9421	0.9361	0.9434	0.9374	0.9447	0.9387	0.9461	0.9400
1	9308	9249	9321	9262	9334	9275	9347	9288	9360	9301	9373	9314	9387	9328	9400	9341	9413	9354	9426	9367
2	9274	9215	9287	9228	9300	9241	9313	9254	9326	9267	9339	9280	9352	9293	9365	9306	9379	9320	9392	9322
3	9240	9181	9253	9194	9266	9207	9279	9220	9292	9233	9305	9246	9318	9259	9331	9272	9344	9285	9357	9287
4	9207	9148	9220	9161	9233	9174	9245	9186	9257	9198	9270	9211	9283	9224	9295	9236	9308	9249	9321	9262
5	0.9174	0.9115	0.9187	0.9128	0.9200	0.9141	0.9213	0.9154	0.9225	0.9166	0.9238	0.9179	0.9251	0.9192	0.9264	0.9205	0.9277	0.9218	0.9290	0.9231
6	9141	9082	9154	9095	9167	9108	9179	9120	9192	9133	9205	9146	9217	9158	9229	9170	9242	9183	9254	9195
7	9108	9049	9121	9062	9133	9074	9145	9086	9157	9098	9170	9111	9183	9124	9195	9136	9208	9149	9221	9162
8	9076	9017	9088	9029	9101	9042	9113	9054	9125	9066	9138	9079	9150	9091	9163	9104	9176	9117	9189	9130
9	9043	8984	9056	8997	9069	9010	9081	9022	9093	9034	9106	9047	9118	9059	9131	9072	9144	9085	9157	9098
10	0.9011	0.8952	0.9024	0.8965	0.9037	0.8978	0.9049	0.8990	0.9062	0.8945	0.9075	0.8958	0.9088	0.8971	0.9100	0.8983	0.9113	0.8996	0.9126	0.9008
11	8980	8921	8992	8933	9005	8946	9017	8958	9029	8970	9042	8983	9054	8995	9067	9008	9080	9021	9093	9034
12	8948	8889	8961	8902	8973	8914	8985	8926	8997	8938	9010	8951	9022	8963	9035	8976	9048	8989	9061	9002
13	8917	8858	8929	8870	8942	8883	8954	8895	8966	8907	8979	8920	8991	8932	9004	8945	9017	8958	9030	8971
14	8886	8827	8898	8839	8911	8852	8923	8864	8935	8876	8948	8889	8961	8902	8973	8914	8986	8927	8999	8940
15	0.8855	0.8796	0.8867	0.8808	0.8880	0.8821	0.8892	0.8833	0.8905	0.8846	0.8918	0.8859	0.8931	0.8872	0.8944	0.8885	0.8957	0.8898	0.9020	0.8961
16	8824	8765	8836	8777	8848	8789	8860	8801	8872	8813	8885	8826	8897	8838	8910	8851	8923	8864	8936	8877
17	8793	8734	8805	8746	8817	8758	8829	8770	8841	8782	8853	8794	8865	8806	8878	8819	8891	8832	8904	8845
18	8763	8704	8776	8717	8788	8729	8800	8741	8812	8753	8824	8765	8836	8777	8848	8789	8861	8802	8874	8815
19	8733	8674	8745	8686	8757	8698	8769	8710	8781	8722	8793	8734	8805	8746	8817	8758	8829	8770	8842	8783
20	0.8703	0.8644	0.8716	0.8657	0.8728	0.8669	0.8740	0.8681	0.8752	0.8693	0.8765	0.8706	0.8777	0.8718	0.8790	0.8731	0.8803	0.8744	0.8816	0.8757
21	8674	8615	8686	8627	8698	8639	8710	8651	8722	8663	8734	8675	8746	8687	8759	8690	8762	8703	8775	8716
22	8644	8585	8656	8597	8668	8609	8680	8621	8692	8633	8704	8645	8716	8657	8728	8669	8741	8682	8754	8695
23	8615	8556	8627	8568	8639	8580	8651	8592	8663	8604	8675	8616	8687	8628	8699	8640	8712	8653	8725	8666
24	8586	8527	8598	8539	8610	8551	8622	8563	8634	8575	8646	8587	8658	8599	8671	8612	8684	8625	8697	8638
25	0.8557	0.8498	0.8569	0.8510	0.8581	0.8522	0.8593	0.8534	0.8605	0.8546	0.8618	0.8559	0.8631	0.8572	0.8644	0.8585	0.8657	0.8598	0.8720	0.8661
26	8528	8469	8540	8481	8552	8493	8564	8505	8575	8516	8588	8529	8600	8541	8612	8553	8625	8566	8638	8579
27	8500	8441	8512	8453	8524	8465	8536	8477	8548	8489	8560	8501	8572	8513	8584	8525	8597	8538	8610	8551
28	8472	8413	8484	8425	8495	8436	8507	8448	8519	8460	8531	8472	8543	8484	8555	8496	8568	8509	8581	8522
29	8443	8384	8455	8396	8467	8408	8479	8420	8491	8432	8503	8444	8515	8456	8527	8468	8540	8481	8553	8494
30	0.8416	0.8357	0.8427	0.8368	0.8439	0.8380	0.8451	0.8392	0.8463	0.8404	0.8475	0.8416	0.8488	0.8429	0.8500	0.8441	0.8513	0.8454	0.8526	0.8467
31	8388	8329	8400	8341	8411	8352	8423	8364	8435	8376	8447	8388	8459	8400	8471	8412	8484	8425	8497	8438
32	8360	8301	8372	8313	8384	8325	8396	8337	8408	8349	8420	8361	8432	8373	8444	8385	8457	8398	8470	8411
33	8333	8274	8345	8286	8356	8297	8368	8309	8380	8321	8392	8333	8404	8345	8416	8357	8429	8370	8442	8383
34	8306	8247	8317	8258	8329	8270	8341	8282	8353	8294	8365	8306	8377	8318	8389	8330	8402	8343	8415	8356
35	0.8279	0.8220	0.8290	0.8231	0.8302	0.8243	0.8314	0.8255	0.8326	0.8267	0.8338	0.8279	0.8350	0.8291	0.8362	0.8303	0.8375	0.8316	0.8388	0.8329
36	8252	8193	8263	8204	8275	8216	8287	8228	8299	8240	8311	8252	8323	8264	8335	8276	8348	8289	8361	8302
37	8225	8166	8237	8178	8248	8189	8260	8201	8272	8213	8284	8225	8296	8237	8308	8249	8321	8262	8334	8275
38	8199	8140	8210	8151	8222	8163	8233	8174	8245	8186	8257	8198	8269	8210	8281	8222	8294	8235	8307	8248
39	8172	8113	8184	8125	8195	8136	8207	8148	8219	8160	8230	8171	8242	8183	8254	8195	8267	8208	8280	8221
40	0.8146	0.8087	0.8158	0.8099	0.8169	0.8110	0.8181	0.8122	0.8193	0.8134	0.8205	0.8146	0.8217	0.8158	0.8229	0.8170	0.8242	0.8183	0.8255	0.8196
41	8120	8061	8132	8073	8143	8084	8155	8096	8167	8108	8179	8120	8191	8132	8203	8144	8216	8157	8229	8170
42	8094	8035	8106	8047	8117	8058	8129	8070	8140	8081	8152	8093	8164	8105	8176	8117	8189	8130	8202	8143
	720		721		722		723		724		725		726		727		728		729	
0	0.9474	0.9415	0.9487	0.9428	0.9500	0.9441	0.9513	0.9454	0.9526	0.9467	0.9539	0.9479	0.9553	0.9						
1	9439	9380	9452	9393	9465	9406	9478	9419	9491	9432	9505	9446	9518							
2	9405	9346	9418	9359	9431	9372	9444	9385	9457	9398	9470	9411	9483							
3	9371	9312	9384	9325	9397	9338	9410	9351	9423	9364	9436	9377	9449							
4	9337	9278	9350	9291	9363	9304	9376	9317	9388	9329	9401	9342	9414							
5	0.9303	0.9244	0.9316	0.9257	0.9329	0.9270	0.9342	0.9283	0.9355	0.9296	0.9368	0.9309	0.9381							
6	9270	9211	9282	9223	9295	9236	9307	9248	9319	9260	9332	9273	9345							
7	9236	9177	9249	9190	9262	9203	9274	9215	9286	9227	9300	9241	9313							
8	9203	9144	9216	9157	9229	9170	9241	9182	925											

Reduction of Gas Volumes

mmHg	750		751		752		753		754		755		756		757		758		759	
	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.
0	0.9868	0.9808	0.9882	0.9821	0.9895	0.9834	0.9908	0.9848	0.9921	0.9861	0.9934	0.9874	0.9947	0.9887	0.9961	0.9900	0.9974	0.9913	0.9987	0.9927
1	9832	9768	9845	9781	9859	9794	9872	9807	9885	9820	9898	9833	9911	9846	9924	9860	9937	9873	9950	9885
2	9797	9732	9810	9746	9823	9758	9836	9771	9849	9780	9862	9793	9875	9806	9888	9819	9901	9832	9914	9845
3	9761	9697	9774	9710	9787	9723	9800	9736	9813	9749	9826	9752	9839	9765	9852	9778	9860	9791	9878	9809
4	9726	9662	9739	9675	9756	9692	9773	9709	9788	9724	9801	9727	9803	9724	9816	9737	9829	9750	9842	9773
5	0.9691	0.9606	0.9704	0.9619	0.9716	0.9632	0.9729	0.9645	0.9742	0.9658	0.9755	0.9671	0.9768	0.9684	0.9781	0.9697	0.9794	0.9709	0.9807	0.9722
6	9656	9566	9669	9578	9682	9591	9694	9604	9707	9617	9720	9630	9733	9643	9746	9656	9759	9669	9772	9685
7	9621	9525	9634	9543	9647	9551	9660	9563	9673	9576	9685	9589	9698	9602	9711	9615	9724	9627	9737	9640
8	9587	9484	9600	9497	9613	9510	9625	9522	9638	9535	9651	9548	9664	9561	9676	9574	9689	9586	9702	9619
9	9553	9443	9566	9456	9578	9469	9591	9481	9604	9494	9617	9507	9629	9520	9642	9532	9655	9545	9668	9581
10	0.9519	0.9402	0.9532	0.9415	0.9544	0.9428	0.9557	0.9440	0.9570	0.9453	0.9583	0.9466	0.9595	0.9478	0.9608	0.9491	0.9621	0.9504	0.9633	0.9546
11	9485	9361	9498	9374	9511	9386	9523	9399	9536	9412	9549	9424	9561	9437	9574	9450	9587	9462	9599	9475
12	9452	9320	9465	9332	9477	9345	9490	9357	9503	9370	9515	9383	9528	9395	9540	9408	9553	9420	9566	9433
13	9419	9278	9432	9291	9444	9303	9457	9316	9469	9328	9482	9341	9494	9353	9507	9366	9520	9378	9532	9391
14	9386	9236	9399	9249	9411	9261	9424	9274	9436	9286	9449	9299	9461	9311	9474	9324	9486	9336	9499	9349
15	0.9354	0.9194	0.9366	0.9206	0.9378	0.9219	0.9391	0.9231	0.9403	0.9244	0.9416	0.9256	0.9428	0.9269	0.9441	0.9281	0.9453	0.9294	0.9466	0.9305
16	9321	9152	9334	9164	9346	9176	9358	9189	9371	9201	9383	9214	9396	9226	9408	9239	9421	9251	9433	9263
17	9289	9109	9301	9121	9314	9134	9326	9146	9338	9158	9351	9171	9363	9183	9376	9196	9388	9208	9400	9222
18	9257	9066	9269	9078	9282	9091	9294	9103	9306	9115	9319	9128	9331	9140	9343	9152	9356	9165	9368	9177
19	9225	9022	9237	9035	9250	9047	9262	9059	9274	9072	9287	9084	9299	9096	9311	9109	9324	9121	9336	9133
20	0.9194	0.8979	0.9206	0.8991	0.9218	0.9003	0.9230	0.9015	0.9243	0.9028	0.9255	0.9040	0.9267	0.9052	0.9279	0.9064	0.9292	0.9077	0.9304	0.9085
21	9162	8934	9175	8947	9187	8959	9199	8971	9211	8983	9223	8996	9236	9008	9248	9020	9260	9032	9272	9044
22	9131	8890	9143	8902	9156	8914	9168	8926	9180	8938	9192	8951	9204	8963	9216	8975	9229	8987	9241	8995
23	9100	8845	9112	8857	9125	8869	9137	8881	9149	8893	9161	8905	9173	8917	9185	8930	9197	8942	9209	8954
24	9070	8799	9082	8811	9094	8823	9106	8835	9118	8847	9130	8859	9142	8872	9154	8884	9166	8896	9178	8908
25	0.9039	0.8753	0.9051	0.8765	0.9063	0.8777	0.9075	0.8789	0.9087	0.8801	0.9099	0.8813	0.9111	0.8825	0.9123	0.8837	0.9136	0.8849	0.9148	0.8851
26	9009	8706	9021	8718	9033	8730	9045	8742	9057	8754	9069	8766	9081	8778	9093	8790	9105	8802	9117	8814
27	8979	8659	8991	8671	9003	8683	9015	8695	9027	8706	9039	8718	9051	8730	9063	8742	9074	8754	9086	8765
28	8949	8611	8961	8623	8973	8634	8985	8646	8997	8658	9008	8670	9020	8682	9032	8694	9044	8706	9056	8718
29	8919	8562	8931	8574	8943	8586	8955	8598	8967	8609	8979	8621	8991	8633	9002	8645	9014	8657	9026	8669
30	0.8890	0.8512	0.8902	0.8524	0.8913	0.8536	0.8925	0.8548	0.8937	0.8560	0.8949	0.8572	0.8961	0.8584	0.8973	0.8595	0.8984	0.8607	0.8996	0.8615
31	8860	8462	8872	8474	8884	8486	8896	8498	8908	8510	8919	8521	8931	8533	8943	8545	8955	8557	8967	8565
32	8831	8411	8843	8423	8855	8435	8867	8447	8878	8458	8890	8470	8902	8482	8914	8494	8925	8506	8937	8517
33	8802	8360	8814	8371	8826	8383	8838	8395	8849	8407	8861	8418	8873	8430	8885	8442	8896	8453	8908	8465
34	8774	8307	8785	8319	8797	8330	8809	8342	8820	8354	8832	8365	8844	8377	8856	8389	8867	8400	8879	8412
35	0.8745	0.8253	0.8757	0.8265	0.8768	0.8277	0.8780	0.8288	0.8792	0.8300	0.8803	0.8312	0.8815	0.8323	0.8827	0.8335	0.8838	0.8347	0.8850	0.8358
36	8717	8199	8728	8210	8740	8222	8752	8234	8763	8245	8775	8257	8786	8269	8798	8280	8810	8292	8821	8303
37	8689	8143	8700	8155	8712	8167	8723	8178	8735	8190	8747	8201	8758	8213	8770	8224	8781	8236	8793	8248
38	8661	8087	8672	8098	8684	8110	8695	8121	8707	8133	8718	8145	8730	8156	8741	8168	8753	8179	8765	8191
39	8633	8029	8644	8041	8656	8052	8667	8064	8679	8075	8690	8087	8702	8098	8713	8110	8725	8121	8736	8133
40	0.8605	0.7970	0.8617	0.7982	0.8628	0.7993	0.8640	0.8005	0.8651	0.8016	0.8663	0.8028	0.8674	0.8039	0.8685	0.8051	0.8697	0.8062	0.8705	0.8074
41	8578	7910	8589	7922	8601	7933	8612	7945	8623	7956	8635	7968	8646	7979	8658	7991	8669	8002	8681	8013
42	8550	7849	8562	7861	8573	7872	8585	7884	8596	7895	8607	7906	8619	7918	8630	7929	8642	7941	8653	7952
mmHg	760		761		762		763		764		765		766		767		768		769	
	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.	dry	sat.
0	1.0000	0.9940	1.0013	0.9953	1.0026	0.9966	1.0039	0.9979	1.0053	0.9992	1.0066	1.0006	1.0079	1.0019	1.0032	0.9972	1.0045	0.9985	1.0058	0.9998
1	0.9963	0.9899	0.9977	0.9912	0.9990	0.9925	0.003	0.9938	0.016	0.9951	0.029	0.9964	0.042	0.9978	0.055	0.9991	0.068	0.9998	0.081	0.9998
2	9927	9858	9940	9871	9953	9884	0.9966	9897	0.9979	9910	0.9992	9923	0.006	9936	0.019	9949	0.032	9956	0.045	9969
3	9891	9817	9904	9830	9917	9843	0.9930	9856	0.9943	9869	0.9956	9882	0.9969	9895	0.009	9908	0.022	9915	0.035	9928
4	9855	9776	9868	9789	9881	9802	9814	9815	9907	9828	9920	9841	9933	9854	9946	9867	9959	9880	0.9972	9893
5	0.9820	0.9735	0.9833	0.9748	0.9846	0.9761	0.9859	0.9774	0.9871	0.9787	0.9884	0.9800	0.9897	0.9813	0.9909	0.9824	0.9915	0.9831	0.9922	0.

The vital functions of highly developed organisms are closely dependent on the internal aqueous medium and on the maintenance in it of extreme constancy of chemical and physical properties. For the physician a knowledge of some of the properties of aqueous solutions is therefore essential to an understanding of water and electrolyte balance and how it may be modified clinically.

In spite of the advances made in physical chemistry there remain considerable gaps in our knowledge of aqueous solutions. The properties of solutions with concentrations up to 0.01 mol/kg can now be calculated with great accuracy, but for solutions of higher concentration it is necessary to introduce empirical correction factors in order to reconcile measured with theoretical values. In biology and medicine, however, this is of little importance since the approximate formulae derived from theory are sufficiently accurate for most practical purposes.

This section should be read in conjunction with the tables on pages 272-276 and with the chapter 'Water and Electrolyte Balance' (pages 523-530).

Definitions of the concepts atom, molecule and ion

A molecule of a substance is that group of elementary particles existing as kinetic unit in the gaseous phase of the substance at low concentration. The number of molecules per unit volume and their kinetic energy determine the mechanical and thermal properties of ideal gases. Molecules can be made up of one kind of element only or of various elements in combination. The smallest part of an element identifiable in compounds of which the element forms a part is known as an atom.

The 'chemical bonds' binding atoms together to form molecules are usually more than one order of magnitude stronger than the attractive forces between molecules. For this reason the molecules of a substance are often recognizable as units even in the condensed state. This does not apply, however, to many groups of substances, in particular metals and salts; here the term molecule is used in the purely formal sense as the sum of the atoms given in the empirical formula.

Salts are not made up of atoms bound together by orientated forces but of electrically charged atoms - known as ions - situated at the centre of a spherically symmetrical electric field. Atoms are transformed into positive ions (cations) by loss of electrons and into negative ions (anions) by capture of electrons. Since the chemical properties of a particle are determined by the number of electrons it possesses, the properties of ions are completely different from those of the corresponding atoms.

Electrolytes

When an electric current is passed through a salt or its solution in water (or other polar solvent) chemical changes occur at the places where the current enters and leaves (the electrodes). This process is known as electrolysis, a substance undergoing it as an electrolyte. Current passing through an electrolyte is carried by material particles, the ions. Positively charged ions (cations), which migrate in the electric field to the cathode, are indicated by one or more plus signs, depending on their valency, placed after their symbol; in the same way negatively charged ions (anions), which migrate to the anode, are indicated by minus signs (for example, magnesium ion = Mg^{2+} , nitrate ion = NO_3^-).

That the ions already exist in the solution and are not formed when the electric field is applied can be demonstrated by measuring properties dependent only on the number of particles present in the solution, such as osmotic pressure, freezing-point depression, etc. (see below). The dissolution of a salt is therefore understood as the statistical distribution of the positive and negative ions forming the solid crystal lattice. This separation of oppositely charged particles is made easier by (1) a higher dielectric constant of the solvent, and (2) a stronger ion-dipole interaction between the ions of the solute and the polar molecules of the solvent (known as solvation or, for water, hydration of the ions). In respect of both (1) and (2) water occupies an almost unique position among solvents.

A solution in which the solute consists of (solvated or hydrated) ions is known as a 'strong' electrolyte (the term electrolyte is also used to describe the solute itself). If ν is the number of ions into which such a solute dissociates, then n mole (see page 226) of the solute will form $n\nu$ mole of particles in solution (positive and negative ions together). Thus for NaCl $\nu = 2$, for $CaCl_2$, $\nu = 3$, while for $K_4Fe(CN)_6$, $\nu = 4$ since $[Fe(CN)_6]^{4-}$ is a single complex ion.

Other substances dissociate in solution partly into ions and partly into molecules. These and their solutions are known as 'weak' electrolytes. They include particularly the weak acids and

bases (almost all organic acids and bases, carbonic acid, hydrogen sulphide, etc.). The fraction of the total number of molecules dissociated into ions is known as the degree of dissociation α . Dissolution of n mole of a weak electrolyte results in the formation of $(\nu\alpha + 1 - \alpha)$ mole of particles. The degree of dissociation α depends to a great extent on the concentration of the solution: the weaker the solution the more complete the dissociation and the closer the degree of dissociation approaches to unity.

Ideal dilute solutions

The thermodynamic treatment of dilute solutions makes use of the concept of the ideal dilute solution. This is a solution in which the molecules of the solute are completely surrounded by solvent molecules, so that any further addition of solvent results in no further interactions between solvent and solute. Under these conditions the properties of the solvent molecules in the solution depend only on the number of dissolved particles and not on their individual properties. Thus the lowering of the vapour pressure of the solvent due to the presence of the solute is proportional to the molar concentration of the solute, and the same applies to the osmotic pressure, freezing-point depression and boiling-point elevation.

The osmotic pressure and freezing-point depression of an ideal dilute aqueous solution are expressed as follows:

$$\text{Osmotic pressure (ideal) in atm} = P_{1d} = 0.082055 \times T \times \frac{M}{V_m} \times m_2 \times \nu \quad (1)$$

$$\text{Freezing-point depression (ideal) in } ^\circ\text{C} = \Delta T_{1d} = 1.86 \times m_2 \times \nu \quad (2)$$

where 0.082055 = the gas constant R in litre atmosphere; T = absolute temperature in kelvin (K) = $273.15 + ^\circ\text{C}$; 1.86 = the cryoscopic constant (molar freezing-point depression of water); m_2 = molality of the solute (number of moles of undissociated solute per 1000 g water); ν = number of particles into which the solute dissociates at complete dissociation (to be replaced by the factor $\nu\alpha + 1 - \alpha$ when dissociation is not complete); M/V_m = ratio of molar mass to molar volume for water (= 1 at a good approximation). For osmotic pressure and freezing-point depression data for osmotic concentrations of 10-740 mmol/1000 g water see page 272.

From (1) and (2) it follows that

$$P_{(\text{atm})} = 0.0441 \times T \times \Delta T \quad (3)$$

$$\text{or } P_{(\text{atm, at } 0^\circ\text{C})} = 12.05 \times \Delta T \quad (4)$$

In contrast to (1) and (2), equations (3) and (4) are valid for a wider range of concentrations than those to which the concept of the ideal dilute solution applies, and for this reason the symbols P and ΔT do not bear the index $1d$ (ideal).

Real solutions

The higher the solute concentration the wider the solution diverges from the concept of the ideal dilute solution. This divergence can be compensated for by means of a correction factor known as the osmotic coefficient g (= 1 for ideal dilute solutions). At any given concentration a real solution diverges the more widely from the ideal solution the stronger the interactions between the particles in it. For ionic solutions the coefficient g is therefore greater than for solutions of undissociated molecules, and for solutions containing multivalent ions it is particularly large.

For very dilute ionic solutions the coefficient g can be calculated by means of the DEBYE-HÜCKEL limiting law. Experimentally, it can be obtained from the relationship

$$g = \frac{\Delta T}{\Delta T_{1d}} = \frac{\Delta T}{1.86 m_2 \nu} \quad (5)$$

where ΔT is the measured freezing-point depression. Most reference books (*International Critical Tables*, *Handbook of Chemistry and Physics*, *Landolt-Börnstein*, etc.) give the latter as a function of the molality m_2 , whence g can be obtained by dividing by 1.86ν in accordance with (5).

In solutions of weak electrolytes the osmotic properties (freezing-point depression, osmotic pressure, etc.) depend mainly on the number of particles, which is a function of the concentration, in other words, they vary with the degree of dissociation α . In this case the divergence from the ideal dilute solution is of importance only in very precise physicochemical measurements, particularly as the ionic concentration remains low.

Measures of concentration

equivalents instead of moles (normality instead of molarity) is always necessary when valency or valency change is involved, particularly in acid-base reactions, oxidations and reductions, but it could be borne in mind that the normality of a solution can differ in different types of reaction (data on decimolal solutions for titrimetric analysis are given on page 277).

Freezing-point depression data are always given for concentrations expressed as molality.

The molality of any particular serum component, its concentration, g/l in mg/l serum, must be converted into its concentration in the serum water.

This conversion can be made by means of either the specific activity or the protein content of serum. The former method is the more accurate and the appropriate factors are given on page 557 in the basis of protein content the conversion is made by means of the following formula:

$$\text{Water content of serum in } g/l \text{ serum} = 934.0 - (0.718 \times \text{protein content in } mg/l \text{ serum}) \quad (6)$$

that is meant by the expression 'molality' in any particular case.

In order to avoid this confusion the molarity and molality should always be related to the undissociated solute, otherwise they should be clearly specified, for instance 'the molality of all osmotically active particles'.

Osmolality, osmolarity

These terms indicate respectively the molarity and molality of an ideal solution of a non-dissociating substance must possess in order to exert the same osmotic pressure as the solution under consideration. Osmolarity and osmolality are not used in the physicochemical field but find considerable application in the sphere of biology and medicine.² As is clear from the definition, the (real) osmolality is a quantity capable of experimental determination. It can also be calculated from the molality of the solution provided (1) the number of molecular fragments (for weak electrolytes the degree of dissociation α) and (2) the correction factor (osmotic coefficient g) from the ideal to the real state are known.

If weak electrolytes are excluded, the ideal osmolality can be obtained by multiplying the molality by the number of molecular fragments. Multiplication of this by the osmotic coefficient g gives the (real) osmolality as defined above.

$$\text{ideal osmolality} = m \times v \quad (7)$$

$$(\text{real}) \text{ osmolality} = \text{ideal osmolality} \times g = m \times v \times g = \Delta T / 1.86 \quad (8)$$

For mixed solutions m_{av} is replaced by the sum $\sum m_i v_i = m_{\text{av}}$ + m_{av} + ... for each of the component solutes. For the sake of simplicity it is assumed that there is no change in the osmotic coefficient when passing from a simple to a mixed solution.

In analogy with the mole, the unit of osmolality and osmolarity is the osmole (osm).

Applications

To obtain freezing-point depression and osmotic pressure from osmolality see the table on page 272.

Osmolality of blood serum from freezing-point depression (0.56°C) (table on page 272).

Columns 5 and 6 of the table show that the (real) osmolality of serum is 302.1 mmol.

Sodium chloride and glucose solutions (table on page 273).

(a) The weights of NaCl and glucose (or fructose) corresponding to given ideal osmolalities are obtained from columns 1/2 and 1/3. Column 7 gives the corresponding caloric values for glucose and fructose.

(b) The ideal osmolalities corresponding to given weights of NaCl and glucose (or fructose) are obtained from columns 11/12 and 11/13. The corresponding caloric values for glucose and fructose are given in column 14.

Water and serum osmolality is 1000 mmol/1000 g water is 1.0893. Since 100 mmol are to be added by means of NaCl, the required weight (see example 4) is $2.922 \times 1.0893 = 3.183 \text{ g NaCl}$.

(d) Isotonic solutions: The concentration required to yield these

References

- WELCH, L.G., in DUNCAN, G.G. (Ed.), *Diagnosis of Metabolism*, 5th ed., Saunders, Philadelphia, 1964, page 447.
- NETTE, H., *Theoretische Biochemie*, Springer, Berlin, 1959, page 108.

Aqueous Solutions – Calculation of Freezing-point Depression and Osmotic Pressure

(For explanation see pages 270-271)

Real osmolality (mmol/1000 g water)	Freezing-point depression ($\Delta T^\circ\text{C}$)	Osmotic pressure		Freezing-point depression ($\Delta T^\circ\text{C}$)	Real osmolality (mmol/1000 g water)	Osmotic pressure	
		at 0°C (atm)	at 38°C* (atm)			at 0°C (atm)	at 38°C* (atm)
1	1	2	4	6	6	7	8
10	0.019	0.22	0.26	0.01	5.4	0.12	0.14
20	0.037	0.45	0.51	02	10.7	0.24	0.28
30	0.056	0.67	0.77	03	16.1	0.36	0.41
40	0.074	0.90	1.01	04	21.5	0.48	0.55
50	0.093	1.12	1.27	05	26.9	0.60	0.69
60	0.112	1.35	1.52	06	32.3	0.72	0.82
70	0.130	1.57	1.78	07	37.6	0.84	0.95
80	0.149	1.79	2.03	08	43.0	0.97	1.09
90	0.167	2.02	2.28	09	48.4	1.09	1.23
100	0.186	2.24	2.54	0.10	53.8	1.21	1.37
10	0.205	2.47	2.79	11	59.2	1.33	1.50
20	0.223	2.69	3.05	12	64.6	1.45	1.64
30	0.242	2.91	3.30	13	70.0	1.57	1.78
40	0.260	3.14	3.55	14	75.3	1.69	1.92
50	0.279	3.36	3.80	0.15	80.7	1.81	2.05
60	0.297	3.59	4.06	16	86.1	1.93	2.18
70	0.316	3.81	4.31	17	91.5	2.05	2.32
80	0.334	4.03	4.57	18	96.9	2.17	2.46
90	0.353	4.26	4.83	19	102.3	2.29	2.59
200	0.371	4.48	5.07	0.20	107.7	2.41	2.73
10	0.390	4.71	5.33	21	113.0	2.53	2.87
20	0.408	4.93	5.58	22	118.4	2.65	3.01
30	0.427	5.16	5.84	23	123.8	2.77	3.14
40	0.445	5.38	6.09	24	129.2	2.89	3.28
50	0.464	5.60	6.34	0.25	134.6	3.02	3.42
60	0.482	5.83	6.59	26	140.0	3.14	3.56
70	0.501	6.05	6.85	27	145.4	3.26	3.68
80	0.519	6.28	7.10	28	150.8	3.38	3.82
90	0.537	6.50	7.36	29	156.2	3.50	3.96
300	0.556	6.72	7.62	0.30	161.6	3.62	4.10
10	0.574	6.95	7.87	31	167.0	3.74	4.23
20	0.593	7.17	8.12	32	172.4	3.86	4.37
30	0.611	7.40	8.37	33	177.8	3.98	4.51
40	0.630	7.62	8.63	34	183.2	4.10	4.65
50	0.648	7.84	8.88	0.35	188.6	4.23	4.78
60	0.667	8.07	9.14	36	194.0	4.35	4.92
70	0.685	8.29	9.39	37	199.4	4.47	5.06
80	0.704	8.52	9.64	38	204.8	4.59	5.20
90	0.722	8.74	9.90	39	210.2	4.71	5.33
400	0.741	8.97	10.15	0.40	215.5	4.84	5.47
10	0.759	9.19	10.40	41	220.9	4.96	5.61
20	0.778	9.41	10.66	42	226.3	5.08	5.75
30	0.796	9.64	10.92	43	231.8	5.20	5.88
40	0.815	9.86	11.16	44	237.2	5.32	6.02
50	0.833	10.09	11.42	0.45	242.6	5.44	6.16
60	0.851	10.31	11.67	46	248.0	5.56	6.30
70	0.870	10.53	11.93	47	253.4	5.68	6.43
80	0.887	10.76	12.17	48	258.8	5.80	6.57
90	0.906	10.98	12.43	49	264.2	5.92	6.71
500	0.925	11.21	12.69	0.50	269.6	6.04	6.85
10	0.943	11.43	12.94	51	275.0	6.16	6.98
20	0.962	11.66	13.20	52	280.4	6.28	7.11
30	0.980	11.88	13.45	53	285.8	6.40	7.25
40	0.998	12.10	13.70	54	291.2	6.52	7.39
50	1.017	12.33	13.95	0.55	296.7	6.64	7.53
60	1.035	12.55	14.21	56	302.1	6.77	7.66
70	1.054	12.78	14.47	57	307.5	6.89	7.80
80	1.072	13.00	14.72	58	312.9	7.02	7.94
90	1.090	13.22	14.97	59	318.3	7.14	8.07
600	1.109	13.45	15.22	0.60	323.7	7.26	8.21
10	1.127	13.67	15.48	61	329.2	7.38	8.35
20	1.146	13.90	15.73	62	334.6	7.49	8.49
30	1.164	14.12	15.99	63	340.0	7.62	8.62
40	1.182	14.34	16.24	64	345.4	7.74	8.76
50	1.201	14.57	16.49	0.65	350.8	7.86	8.90
60	1.219	14.79	16.75	66	356.2	7.98	9.04
70	1.238	15.02	17.00	67	361.6	8.10	9.17
80	1.256	15.24	17.26	68	367.0	8.22	9.31
90	1.274	15.47	17.51	69	372.5	8.34	9.45
700	1.292	15.69	17.77	0.70	377.9	8.47	9.59
10	1.311	15.91	18.01	71	383.3	8.59	9.72
20	1.329	16.14	18.27	72	388.7	8.71	9.86
30	1.347	16.36	18.52	73	394.2	8.84	10.00
40	1.365	16.59	18.78	74	399.6	8.96	10.14

* Normal blood temperature = ca. 38°C = 311.15 K.

(For explanation see page 271)

Values in columns 3-5 and 8-10 have been calculated for the osmolalities in column 1 read as real osmotic concentrations (millimoles or grammes per 100 g water). The osmotic coefficients ϕ have been obtained by interpolation from the data of SEATCHARD and PARENTIS, *J. Amer. Chem. Soc.*, 55, 4355 (1933), for NaCl and ROTH, W. A., *Z. phys. Chem.*, 43, 539 (1903), for glucose.

Common salt (NaCl, mol wt 58.443)										D-Glucose* (C ₆ H ₁₂ O ₆ , mol wt 180.16)										Common salt (NaCl)		D-Glucose* (C ₆ H ₁₂ O ₆)	
Osmolality (ideal)	Corresponds to a weight of	Weight necessary when the amount in column 1 is added to bring the total osmolality to 300 mmol	Osmotic coefficient corresponding to the osmolality in column 1 read as real osmolality	Corresponds to a weight of	Corresponds to a caloric value of	Weight necessary when the amount in column 1 is added to bring the total osmolality to 300 mmol	Osmotic coefficient corresponding to the osmolality in column 1 read as real osmolality	Corresponds to a weight of	Corresponds to a caloric value of	Weight necessary when the amount in column 1 is added to bring the total osmolality to 300 mmol	Osmotic coefficient corresponding to the osmolality in column 1 read as real osmolality	Corresponds to a weight of	Corresponds to a caloric value of	Weight necessary when the amount in column 1 is added to bring the total osmolality to 300 mmol	Osmotic coefficient corresponding to the osmolality in column 1 read as real osmolality	Corresponds to an ideal osmolality of	Corresponds to an ideal osmolality of	Corresponds to a caloric value of					
mmol	g	g	ϕ	1/g	g	cal**	ϕ	g	cal**	g	ϕ	g	cal**	g	ϕ	mmol	mmol	cal**					
1	1	1			1			1		1		1		1		1	1	1					
10	0.292	0.315	0.9778	1.0227	1.802	7.53	1.777	1.0005	0.9995	1	34.22	5.55	1.18										
20	0.584	0.630	0.9703	1.0305	3.603	15.07	3.554	1.0009	0.9991	2	68.44	11.10	2.36										
30	0.877	0.947	0.9653	1.0359	5.405	22.60	5.331	1.0014	0.9986	3	102.65	16.65	3.53										
40	1.169	1.262	0.9612	1.0404	7.206	30.14	7.108	1.0018	0.9982	4	136.89	22.20	4.71										
50	1.461	1.577	0.9579	1.0440	9.008	37.67	8.885	1.0023	0.9977	5	171.11	27.75	5.91										
60	1.753	1.922	0.9550	1.0471	10.810	45.21	10.662	1.0028	0.9972	6	205.33	33.30	7.09										
70	2.046	2.208	0.9525	1.0499	12.611	52.74	12.439	1.0032	0.9968	7	239.55	38.85	8.27										
80	2.338	2.524	0.9503	1.0523	14.413	60.27	14.217	1.0037	0.9963	8	273.77	44.41	9.44										
90	2.630	2.839	0.9482	1.0546	16.214	67.81	15.994	1.0041	0.9959	9	307.99	49.96	10.62										
100	2.922	3.154	0.9463	1.0567	18.016	75.34	17.771	1.0046	0.9954	10	342.22	55.51	11.80										
110	3.214	3.469	0.9448	1.0584	19.818	82.88	19.548	1.0050	0.9949	11	376.44	61.06	12.98										
120	3.507	3.785	0.9431	1.0602	21.619	90.41	21.325	1.0055	0.9945	12	410.66	66.61	14.16										
130	3.799	4.101	0.9418	1.0618	23.421	97.95	23.102	1.0060	0.9940	13	444.88	72.16	15.34										
140	4.091	4.416	0.9405	1.0633	25.222	105.48	24.879	1.0064	0.9936	14	479.10	77.71	16.52										
150	4.383	4.731	0.9392	1.0647	27.024	113.01	26.656	1.0069	0.9931	15	513.32	83.26	17.70										
160	4.675	5.047	0.9380	1.0661	28.826	120.55	28.433	1.0074	0.9927	16	547.54	88.81	18.88										
170	4.968	5.362	0.9368	1.0675	30.627	128.08	30.210	1.0078	0.9923	17	581.77	94.36	20.06										
180	5.260	5.678	0.9357	1.0687	32.429	135.62	31.987	1.0083	0.9918	18	615.99	99.91	21.24										
190	5.552	5.993	0.9347	1.0699	34.230	143.15	33.764	1.0087	0.9914	19	650.21	105.46	22.42										
200	5.844	6.308	0.9337	1.0710	36.032	150.68	35.541	1.0092	0.9909	20	684.43	111.01	23.60										
210	6.137	6.624	0.9328	1.0720	37.834	158.22	37.318	1.0097	0.9904	21	718.65	116.56	24.78										
220	6.429	6.939	0.9319	1.0731	39.635	165.75	39.096	1.0101	0.9900	22	752.87	122.11	25.96										
230	6.721	7.255	0.9311	1.0741	41.437	173.28	40.873	1.0106	0.9895	23	787.09	127.66	27.14										
240	7.013	7.570	0.9304	1.0748	43.238	180.82	42.650	1.0110	0.9891	24	821.32	133.22	28.32										
250	7.305	7.885	0.9297	1.0756	45.040	188.35	44.427	1.0115	0.9886	25	855.54	138.77	29.50										
260	7.598	8.201	0.9290	1.0764	46.842	195.89	46.204	1.0120	0.9881	26	889.76	144.32	30.68										
270	7.890	8.516	0.9283	1.0772	48.644	203.42	47.981	1.0124	0.9877	27	923.98	149.87	31.86										
280	8.182	8.832	0.9276	1.0780	50.445	210.96	49.758	1.0129	0.9873	28	958.20	155.42	33.04										
290	8.474	9.147	0.9270	1.0787	52.246	218.49	51.535	1.0133	0.9869	29	992.42	160.97	34.22										
300	8.766	9.463	0.9264	1.0794	54.048	226.03	53.312	1.0138	0.9864	30	1026.65	166.52	35.40										
310	9.057	9.778	0.9258	1.0801	55.850	233.56	55.089	1.0143	0.9860	31	1060.87	172.07	36.58										
320	9.351	10.093	0.9252	1.0808	57.651	241.10	56.866	1.0147	0.9855	32	1095.09	177.62	37.76										
330	9.643	10.408	0.9246	1.0815	59.453	248.63	58.643	1.0152	0.9851	33	1129.32	183.17	38.94										
340	9.935	10.723	0.9241	1.0821	61.255	256.17	60.420	1.0156	0.9846	34	1163.54	188.72	40.12										
350	10.228	11.038	0.9236	1.0827	63.056	263.70	62.197	1.0161	0.9842	35	1197.77	194.27	41.30										
360	10.520	11.353	0.9232	1.0832	64.858	271.23	63.974	1.0165	0.9837	36	1231.99	199.82	42.48										
370	10.812	11.668	0.9227	1.0838	66.659	278.77	65.751	1.0170	0.9833	37	1266.21	205.37	43.66										
380	11.104	11.983	0.9223	1.0843	68.461	286.30	67.528	1.0175	0.9828	38	1300.43	210.92	44.84										
390	11.396	12.298	0.9219	1.0847	70.262	293.84	69.305	1.0179	0.9824	39	1334.65	216.47	46.02										
400	11.689	12.613	0.9215	1.0852	72.064	301.37	71.082	1.0183	0.9820	40	1368.87	222.02	47.20										
410	11.981	12.928	0.9211	1.0857	73.866	308.91	72.859	1.0187	0.9816	41	1403.09	227.57	48.38										
420	12.273	13.243	0.9207	1.0861	75.667	316.44	74.636	1.0192	0.9812	42	1437.31	233.12	49.56										
430	12.565	13.558	0.9203	1.0866	77.469	323.98	76.413	1.0196	0.9808	43	1471.53	238.67	50.74										
440	12.857	13.873	0.9200	1.0869	79.270	331.51	78.190	1.0201	0.9803	44	1505.75	244.22	51.92										
450	13.150	14.188	0.9196	1.0874	81.072	339.04	80.000	1.0205	0.9799	45	1539.97	249.77	53.10										
460	13.442	14.503	0.9192	1.0878	82.874	346.58	81.811	1.0209	0.9795	46	1574.19	255.32	54.28										
470	13.734	14.818	0.9188	1.0882	84.675	354.11	83.622	1.0214	0.9790	47	1608.41	260.87	55.46										
480	14.026	15.133	0.9185	1.0887	86.477	361.64	85.433	1.0218	0.9787	48	1642.63	266.42	56.64										
490	14.319	15.448	0.9182	1.0891	88.278	369.18	87.244	1.0222	0.9783	49	1676.85	271.97	57.82										
500	14.611	15.763	0.9180	1.0893	90.080	376.72	89.055	1.0226	0.9779	50	1711.07	277.52	59.00										
510	14.903	16.078	0.9177	1.0897	91.882	384.25	90.866	1.0230	0.9775	51	1745.29	283.07	60.18										
520	15.195	16.393	0.9174	1.0900	93.684	391.79	92.677	1.0234	0.9771	52	1779.51	288.62	61.36										
530	15.487	16.708	0.9172	1.0903	95.485	399.32	94.488	1.0238	0.9767	53	1813.73	294.17	62.54										
540	15.780	17.023	0.9170	1.0905	97.286	406.86	96.299	1.0242	0.9764	54	1847.95	299.72	63.72										
550	16.072	17.338	0.9167	1.0908	99.088	414.39	98.110	1.0245	0.9761	55	1882.17	305.27	64.90										
560	16.364	17.653	0.9165	1.0911	100.890	421.92	99.921	1.0249	0.9757	56	1916.40	310.82	66.08										
570	16.656	17.968	0.9163	1.0913	102.691	429.45	101.732	1.0253	0.9753	57	1950.62	316.37	67.26										
580	16.948	18.283	0.9161	1.0916	104.493	436.98	103.543	1.0256	0.9750	58	1984.85	321.92	68.44										
590	17.240	18.598	0.9159	1.0919	106.294	444.52	105.354	1.0260	0.9747	59	2019.07	327.47	69.62										
600	17.532	18.913	0.9157	1.0921	108.096	452.05	107.165	1.0263	0.9744	60	2053.29	333.02	70.80										
610	17.825	19.228	0.9155	1.0923	109.898	459.59	108.976	1.0267	0.9740	61	2087.51	338.57	71.98										
620	18.117	19.543	0.9153	1.0925	111.699	467.12	110.787	1.0270	0.9737	62	2121.73	344.12	73.16										
630	18.410	19.858	0.9152	1.0927	113.501	474.66	112.598	1.0274	0.9734	63	2155.95	349.67	74.34										
640	18.702	20.173	0.9150	1.0929	115.302	482.19	114.409																

Aqueous Solutions - Conversion Factors for Electrolytes (I)

Electrolyte (data for 1 g unless otherwise stated)			Molecular weight	Undissociated solute mmol	Solubility† (gramme per 1000 ml water)		Cation			Anion			Millimoles††
					cold	hot	mEq	mg		mEq	mg		
Calcium (Ca)													
1	acetate	Ca(C ₂ H ₃ O ₂) ₂ + H ₂ O	176.19	5.68	436 ³⁰	331 ¹⁰⁰	11.35	227	Ca ⁺⁺	11.35	670	C ₂ H ₃ O ₂ ⁻	17.03
2		Ca(C ₂ H ₃ O ₂) ₂ + 2 H ₂ O	194.20	5.15	459 ⁹	411 ⁸⁰	10.30	206	Ca ⁺⁺	10.30	608	C ₂ H ₃ O ₂ ⁻	15.43
3	chloride	CaCl ₂ + 2 H ₂ O	147.02	6.80	1812 ⁸⁰	2106 ¹⁰⁰	13.60	273	Ca ⁺⁺	13.60	482	Cl ⁻	20.43
4		CaCl ₂ + 6 H ₂ O	219.08	4.56	1175 ⁹	2013 ³⁰	9.13	183	Ca ⁺⁺	9.13	324	Cl ⁻	13.69
5	citrate	Ca ₃ (C ₆ H ₅ O ₇) ₂ + 4 H ₂ O	570.51	1.75	8.5 ¹⁸	9.6 ²³	10.52	211	Ca ⁺⁺	10.52	663	C ₆ H ₅ O ₇ ⁻⁻⁻	8.76
6	D-glucuronate	Ca(C ₆ H ₁₁ O ₇) ₂ + H ₂ O	448.40	2.23	33 ¹⁸		4.46	89	Ca ⁺⁺	4.46	870	C ₆ H ₁₁ O ₇ ⁻	6.69
7	lactate	Ca(C ₃ H ₅ O ₃) ₂ + 5 H ₂ O	308.30	3.24	31 ⁹	79 ³⁰	6.49	130	Ca ⁺⁺	6.49	578	C ₃ H ₅ O ₃ ⁻	9.23
8	lactulinate	Ca(C ₅ H ₇ O ₅) ₂ + 2 H ₂ O	306.33	3.26	400		6.53	131	Ca ⁺⁺	6.53	752	C ₅ H ₇ O ₅ ⁻	9.79
9	oxide (lime)*	CaO	56.08	17.83	1.31 ^{10d}	0.7 ^{80d}	35.66	715	Ca ⁺⁺				
10	phosphate, dibasic	CaHPO ₄ + 2 H ₂ O	172.09	5.81	0.2 ²⁵	0.75 ¹⁰⁰	11.62	233	Ca ⁺⁺	11.62	558/180	HPO ₄ ⁻⁻ / P	11.62
11	thiosulphate	CaS ₂ O ₃ + 6 H ₂ O	260.30	3.84	1000 ⁹	d	7.68	154	Ca ⁺⁺	7.68	431/246	S ₂ O ₃ ⁻⁻ / S	7.68
Chlorine (Cl)													
12	Ammonium chloride	NH ₄ Cl	53.49	18.69	294 ⁹	773 ¹⁰⁰	18.69	337	NH ₄ ⁺	18.69	663	Cl ⁻	37.39
13	Hydrochloric acid (10% solution)												
	1 g	(0.1 g HCl)	36.46	2.74	∞	∞	2.74	2.8	H ⁺	2.74	97.2	Cl ⁻	5.45
	1 ml	(0.1047 g HCl)	36.46	2.87	∞	∞	2.87	2.9	H ⁺	2.87	101.8	Cl ⁻	5.74
See also Calcium (3, 4), Magnesium (14, 15), Potassium (22) and Sodium (35)													
Magnesium (Mg)													
14	chloride	MgCl ₂	95.21	10.50	542.5 ²⁰	727 ¹⁰⁰	21.00	255	Mg ⁺⁺	21.0	745	Cl ⁻	31.50
15		MgCl ₂ + 6 H ₂ O	203.30	4.92	1127 ⁹	1559 ¹⁰⁰	9.84	120	Mg ⁺⁺	9.84	349	Cl ⁻	14.75
16	hydroxide	Mg(OH) ₂	58.32	17.14	0.009 ¹⁸	0.04 ¹⁰⁰	34.29	417	Mg ⁺⁺				
17	oxide (magnesia)*	MgO	40.30	24.80	0.0062	0.086 ³⁰	49.60	603	Mg ⁺⁺				
18	sulphate (Epsom salt)	MgSO ₄ + 7 H ₂ O	246.47	4.06	483 ¹⁰	641 ⁴⁰	8.11	98.6	Mg ⁺⁺	8.11	390/130	SO ₄ ⁻⁻ / S	8.11
Phosphorus (P)													
See Calcium (10), Potassium (26, 27) and Sodium (30, 31, 40-42)													
Potassium (K)													
19	acetate	K(C ₂ H ₃ O ₂)	98.15	10.19	2530 ²⁰	4920 ⁶²	10.19	398	K ⁺	10.19	602	C ₂ H ₃ O ₂ ⁻	20.38
20	bicarbonate	KHCO ₃	100.12	9.99	183 ⁹	375 ⁸⁰	9.99	391	K ⁺	9.99	609	HCO ₃ ⁻	19.98
21	bromide	KBr	119.01	8.40	535 ⁹	1040 ¹⁰⁰	8.40	329	K ⁺	8.40	671	Br ⁻	16.81
22	chloride	KCl	74.56	13.41	276 ⁹	567 ¹⁰⁰	13.41	524	K ⁺	13.41	476	Cl ⁻	26.83
23	citrate	K ₃ (C ₆ H ₅ O ₇) + H ₂ O	324.42	3.08	1670 ¹⁵	1997 ²¹	9.25	362	K ⁺	9.25	583	C ₆ H ₅ O ₇ ⁻⁻⁻	12.35
24	D-glucuronate	K(C ₆ H ₁₁ O ₇)	234.25	4.27			4.27	167	K ⁺	4.27	833	C ₆ H ₁₁ O ₇ ⁻	8.54
25	oxide*	K ₂ O	94.20	10.62	d	d	21.23	830					
26	phosphate, monobasic	KH ₂ PO ₄	136.09	7.35	330 ²³	v.s.	7.35	287	K ⁺	14.70	705/228	HPO ₄ ⁻⁻ / P	22.04
27	phosphate, dibasic	K ₂ HPO ₄	174.18	5.74	1670 ²⁰	v.s.	11.48	449	K ⁺				
Sodium (Na)													
28	acetate	Na(C ₂ H ₃ O ₂) + 3 H ₂ O	136.08	7.35	602 ⁹	2306 ⁸⁰	7.35	169	Na ⁺	7.35	434	C ₂ H ₃ O ₂ ⁻	14.70
29	acid citrate	Na ₃ H(C ₆ H ₅ O ₇) + 1½ H ₂ O	263.11	3.80	v.s.	v.s.	7.60	175	Na ⁺	7.60	723	H(C ₆ H ₅ O ₇) ⁻	11.43
							7.60	175	Na ⁺	11.4	719	C ₆ H ₅ O ₇ ⁻⁻⁻	15.23
							3.80	3.83	H ⁺				
30	acid phosphate	NaH ₂ PO ₄ + H ₂ O	137.99	7.25	599 ⁹	1824 ⁵⁰	7.25	167	Na ⁺	14.49	696/224	HPO ₄ ⁻⁻ / P	21.74
							7.25	7.3	H ⁺				
31		NaH ₂ PO ₄ + 2 H ₂ O	156.01	6.41	753 ⁹	1797 ⁴⁰	6.41	147	Na ⁺	12.82	615/199	HPO ₄ ⁻⁻ / P	19.23
							6.41	6.5	H ⁺				
32	aminosalicylate	Na(C ₇ H ₅ O ₃ N) + 2 H ₂ O	211.15	4.74			4.74	109	Na ⁺	4.74	720	C ₇ H ₅ O ₃ N ⁻	9.47
33	bicarbonate**	NaHCO ₃	84.01	11.90	69 ⁹	164 ⁸⁰	11.90	274	Na ⁺	11.90	726	HCO ₃ ⁻	23.81
34	bromide	NaBr	102.89	9.72	542 ⁸⁰	548 ¹⁰⁰	9.72	223	Na ⁺	9.72	777	Br ⁻	19.44
35	chloride (common salt)	NaCl	58.44	17.11	357 ⁹	398 ¹⁰⁰	17.11	393	Na ⁺	17.11	607	Cl ⁻	34.22
36	citrate	Na ₃ (C ₆ H ₅ O ₇) + 2 H ₂ O	294.10	3.40	720 ²⁵	1670 ¹⁰⁰	10.19	235	Na ⁺	10.19	643	C ₆ H ₅ O ₇ ⁻⁻⁻	13.60
37		Na ₃ (C ₆ H ₅ O ₇) + 5½ H ₂ O	357.16	2.80	926 ²⁵	2500 ¹⁰⁰	8.40	193	Na ⁺	8.40	529	C ₆ H ₅ O ₇ ⁻⁻⁻	11.20
38	lactate**	Na(C ₃ H ₅ O ₃)	112.06	8.92	v.s.		8.92	205	Na ⁺	8.92	795	C ₃ H ₅ O ₃ ⁻	17.84
39	oxide*	Na ₂ O	61.98	16.13	d	d	32.26	742	Na ⁺				
40	phosphate	Na ₂ HPO ₄	141.96	7.04		1022 ¹⁰⁰	14.09	324	Na ⁺	14.09	676/218	HPO ₄ ⁻⁻ / P	21.13
41		Na ₂ HPO ₄ + 2 H ₂ O	177.99	5.62	1006 ⁵⁰	1290 ⁸⁰	11.24	258	Na ⁺	11.24	539/174	HPO ₄ ⁻⁻ / P	16.95
42		Na ₂ HPO ₄ + 12 H ₂ O	358.14	2.79	42.1 ⁹	525 ⁵⁰	5.58	128	Na ⁺	5.58	268/86.5	HPO ₄ ⁻⁻ / P	8.58
43	salicylate	Na(C ₇ H ₅ O ₃)	160.11	6.25	1110 ¹⁵	1250 ²⁵	6.25	144	Na ⁺	6.25	856	C ₇ H ₅ O ₃ ⁻	12.47
44	sulphate (anhydrous)	Na ₂ SO ₄	142.04	7.04	488 ⁶⁰	425 ¹⁰⁰	14.08	324	Na ⁺	14.08	676/226	SO ₄ ⁻⁻ / S	21.13
45	sulphate (Glauber's salt)	Na ₂ SO ₄ + 10 H ₂ O	322.19	3.10	113 ⁹	925 ⁵⁰	6.21	143	Na ⁺	6.21	298/100	SO ₄ ⁻⁻ / S	9.31
46	thiosulphate	Na ₂ S ₂ O ₃	158.11	6.32	525 ⁹	2660 ¹⁰⁰	12.65	291	Na ⁺	12.65	709/406	S ₂ O ₃ ⁻⁻ / S	16.67
Sulphur (S)													
See Calcium (11), Magnesium (18) and Sodium (44-46)													

+ The index figures are the temperatures in °C; v.s. = very soluble;
d = decomposes.

†† On the assumption of complete dissociation.

* The oxides have been included in view of the continuing use of the older
names.

** The sodium content of 1 g sodium bicarbonate corresponds to that of 1.33 g sodium lactate. The sodium content of 1 g sodium lactate corresponds to that of 0.75 g sodium bicarbonate.

Electrolyte (data for 10 moem of solute* unless otherwise stated)			Undissociated solute		Canon			Anion		
			g	mmol	mEq	mg		mEq	mg	
Calcium (Ca)										
1	acetate	$\text{Ca}(\text{C}_2\text{H}_3\text{O}_2)_2 + \text{H}_2\text{O}$	0.587	3%	6%	134	Ca^{++}	6%	394	$\text{C}_2\text{H}_3\text{O}_2^-$
2		$\text{Ca}(\text{C}_2\text{H}_3\text{O}_2)_2 + 2\text{H}_2\text{O}$	0.647	3%	6%	134	Ca^{++}	6%	394	$\text{C}_2\text{H}_3\text{O}_2^-$
3	chloride	$\text{CaCl}_2 + 2\text{H}_2\text{O}$	0.490	3%	6%	134	Ca^{++}	6%	236	Cl^-
4		$\text{CaCl}_2 + 6\text{H}_2\text{O}$	0.730	3%	6%	134	Ca^{++}	6%	236	Cl^-
5	citrate	$\text{Ca}_3(\text{C}_6\text{H}_5\text{O}_7)_2 + 4\text{H}_2\text{O}$	1.141	2	12	240	Ca^{++}	12	756	$\text{C}_6\text{H}_5\text{O}_7^{---}$
6	D-glucosate	$\text{Ca}(\text{C}_6\text{H}_{11}\text{O}_6)_2 + \text{H}_2\text{O}$	1.495	3%	6%	134	Ca^{++}	6%	1301	$\text{C}_6\text{H}_{11}\text{O}_6^-$
7	lactate	$\text{Ca}(\text{C}_3\text{H}_5\text{O}_2)_2 + 5\text{H}_2\text{O}$	1.028	3%	6%	134	Ca^{++}	6%	594	$\text{C}_3\text{H}_5\text{O}_2^-$
8	laevulinate	$\text{Ca}(\text{C}_6\text{H}_7\text{O}_6)_2 + 2\text{H}_2\text{O}$	1.021	3%	6%	134	Ca^{++}	6%	767	$\text{C}_6\text{H}_7\text{O}_6^-$
9	phosphate, dibasic	$\text{CaHPO}_4 + 2\text{H}_2\text{O}$	0.860	5	10	200	Ca^{++}	10	480	HPO_4^{--}
									155	P
1	thiouraphate	$\text{CaS}_2\text{O}_3 + 6\text{H}_2\text{O}$	1.302	5	10	200	Ca^{++}	10	561	$\text{S}_2\text{O}_3^{--}$
									321	S
Chlorine (Cl)										
2	Ammonium chloride	NH_4Cl	0.267	5	5	90	NH_4^+	5	177	Cl^-
3	Hydrochloric acid (10% solution)									
	1 g	(0.1 g HCl/g)	1.823	5	5	5	H^+	5	177	Cl^-
	1 ml	(0.1047 g HCl/ml)	1.741	5	5	5	H^+	5	177	Cl^-
See also Calcium (3, 4), Magnesium (14, 15), Potassium (22) and Sodium (13)										
Magnesium (Mg)										
14	chloride	MgCl_2	0.317	3%	6%	81	Mg^{++}	6%	236	Cl^-
15		$\text{MgCl}_2 + 6\text{H}_2\text{O}$	0.678	3%	6%	81	Mg^{++}	6%	236	Cl^-
15	sulphate	$\text{MgSO}_4 + 7\text{H}_2\text{O}$	1.232	5	10	122	Mg^{++}	10	480	SO_4^{--}
									160	S
Phosphorus (P)										
See Calcium (10), Potassium (24, 27) and Sodium (10, 31, 40-42)										
Potassium (K)										
19	acetate	$\text{K}(\text{C}_2\text{H}_3\text{O}_2)$	0.491	5	5	196	K^+	5	295	$\text{C}_2\text{H}_3\text{O}_2^-$
20	bicarbonate	KHCO_3	0.501	5	5	196	K^+	5	305	HCO_3^-
21	bromide	KBr	0.595	5	5	196	K^+	5	400	Br^-
22	chloride	KCl	0.573	5	5	196	K^+	5	177	Cl^-
23	citrate	$\text{K}_3(\text{C}_6\text{H}_5\text{O}_7) + \text{H}_2\text{O}$	0.811	2%	7%	293	K^+	7%	473	$\text{C}_6\text{H}_5\text{O}_7^{---}$
24	D-glucosate	$\text{K}(\text{C}_6\text{H}_{11}\text{O}_6)$	1.171	5	5	196	K^+	5	976	$\text{C}_6\text{H}_{11}\text{O}_6^-$
26	phosphate, monobasic	KH_2PO_4	0.454	3%	3%	130	K^+	6%	320	HPO_4^{--}
									103	P
27	phosphate, dibasic	K_2HPO_4	0.581	3%	6%	261	K^+	6%	320	HPO_4^{--}
									103	P
Sodium (Na)										
28	acetate	$\text{Na}(\text{C}_2\text{H}_3\text{O}_2) + 3\text{H}_2\text{O}$	0.680	5	5	115	Na^+	5	295	$\text{C}_2\text{H}_3\text{O}_2^-$
29	acid citrate	$\text{Na}_2\text{H}(\text{C}_6\text{H}_5\text{O}_7) + \frac{1}{2}\text{H}_2\text{O}$	0.656	2%	5	115	Na^+	7%	473	$\text{C}_6\text{H}_5\text{O}_7^{---}$
30	acid phosphate	$\text{NaH}_2\text{PO}_4 + \text{H}_2\text{O}$	0.460	3%	3%	77	Na^+	6%	320	HPO_4^{--}
31		$\text{NaH}_2\text{PO}_4 + 2\text{H}_2\text{O}$	0.520	3%	3%	77	Na^+	6%	320	HPO_4^{--}
									103	P
32	aminosalicylate	$\text{Na}(\text{C}_7\text{H}_5\text{O}_2\text{N}) + 2\text{H}_2\text{O}$	1.056	5	5	115	Na^+	5	761	$\text{C}_7\text{H}_5\text{O}_2\text{N}^-$
33	bicarbonate	NaHCO_3	0.420	5	5	115	Na^+	5	305	HCO_3^-
34	bromide	NaBr	0.514	5	5	115	Na^+	5	400	Br^-
35	chloride	NaCl	0.292	5	5	115	Na^+	5	177	Cl^-
36	citrate	$\text{Na}_3(\text{C}_6\text{H}_5\text{O}_7) + 2\text{H}_2\text{O}$	0.735	2%	7%	172	Na^+	7%	473	$\text{C}_6\text{H}_5\text{O}_7^{---}$
37		$\text{Na}_3(\text{C}_6\text{H}_5\text{O}_7) + 5\frac{1}{2}\text{H}_2\text{O}$	0.893	2%	7%	172	Na^+	7%	473	$\text{C}_6\text{H}_5\text{O}_7^{---}$
38	lactate	$\text{Na}(\text{C}_3\text{H}_5\text{O}_2)$	0.560	5	5	115	Na^+	5	445	$\text{C}_3\text{H}_5\text{O}_2^-$
40	phosphate	Na_2HPO_4	0.473	3%	6%	153	Na^+	6%	320	HPO_4^{--}
									103	P
41		$\text{Na}_2\text{HPO}_4 + 2\text{H}_2\text{O}$	0.593	3%	6%	153	Na^+	6%	320	HPO_4^{--}
									103	P
42		$\text{Na}_2\text{HPO}_4 + 12\text{H}_2\text{O}$	1.194	3%	6%	153	Na^+	6%	320	HPO_4^{--}
									103	P
43	salicylate	$\text{Na}(\text{C}_7\text{H}_5\text{O}_2)$	0.801	5	5	115	Na^+	5	686	$\text{C}_7\text{H}_5\text{O}_2^-$
44	sulphate (anhydrous)	Na_2SO_4	0.473	3%	6%	153	Na^+	6%	320	SO_4^{--}
									107	S
45	sulphate	$\text{Na}_2\text{SO}_4 + 10\text{H}_2\text{O}$	1.074	3%	6%	153	Na^+	6%	320	SO_4^{--}
									107	S
46	thiouraphate	$\text{Na}_2\text{S}_2\text{O}_3$	0.527	3%	6%	153	Na^+	6%	374	$\text{S}_2\text{O}_3^{--}$
									214	S
Sulphur (S)										
See Calcium (11), Magnesium (18) and Sodium (44-46)										

* On the assumption of complete dissociation

Aqueous Solutions - Conversion Factors for Electrolytes (III)

Left-hand column: Given: weight of the inorganic ions. Required: corresponding weight of the salt.
Right-hand column: Given: milliequivalents of the ions. Required: corresponding weight of the salt.

Inorganic Ions		
1	1 g = 49.90 mEq Calcium (Ca ⁺⁺) corresponds to	1 mEq = 20.04 mg Calcium (Ca ⁺⁺) corresponds to
2	4.396 g Calcium acetate	88.09 mg Calcium acetate
3	4.845 g Calcium acetate dihydrate	97.10 mg Calcium acetate dihydrate
4	3.668 g Calcium chloride	73.51 mg Calcium chloride
5	5.466 g Calcium chloride hexahydrate	109.54 mg Calcium chloride hexahydrate
6	4.745 g Calcium citrate	95.08 mg Calcium citrate
7	11.188 g Calcium D-gluconate	224.20 mg Calcium D-gluconate
8	7.692 g Calcium lactate	154.15 mg Calcium lactate
9	7.643 g Calcium laevulinate	153.17 mg Calcium laevulinate
11	4.294 g Calcium phosphate, dibasic	86.05 mg Calcium phosphate, dibasic
12	6.495 g Calcium thiosulphate	130.15 mg Calcium thiosulphate
	1 g Carbon dioxide (CO ₂) corresponds to 1.387 g = 22.72 mEq bicarbonate ions (HCO ₃ ⁻)	1 mEq = 61.02 mg Bicarbonate ions (HCO ₃ ⁻) corresponds to 44.01 mg carbon dioxide (CO ₂)
	1 vol% Carbon dioxide (CO ₂) at 0 °C and 760 mm Hg corresponds to 27.41 mg/l = 0.449 mEq/l bicarbonate ions (HCO ₃ ⁻)*	1 mEq/l = 61.02 mg/l Bicarbonate ions (HCO ₃ ⁻) corresponds to 0 °C and 760 mm Hg to 2.23 vol% carbon dioxide (CO ₂)*
13	1 g = 28.21 mEq Chloride (Cl ⁻) corresponds to	1 mEq = 35.453 mg Chloride (Cl ⁻) corresponds to
14	1.509 g Ammonium chloride	53.49 mg Ammonium chloride
4	2.073 g Calcium chloride	73.51 mg Calcium chloride
5	3.090 g Calcium chloride hexahydrate	109.55 mg Calcium chloride hexahydrate
15	10.28 g or 9.823 ml Hydrochloric acid 10%	364.6 mg or 348.24 µl Hydrochloric acid 10%
17	1.343 g Magnesium chloride	47.61 mg Magnesium chloride
18	2.867 g Magnesium chloride hexahydrate	101.66 mg Magnesium chloride hexahydrate
27	2.103 g Potassium chloride	74.56 mg Potassium chloride
41	1.648 g Sodium chloride	58.44 mg Sodium chloride
16	1 g = 82.3 mEq Magnesium (Mg ⁺⁺) corresponds to	1 mEq = 12.15 mg Magnesium (Mg ⁺⁺) corresponds to
17	3.917 g Magnesium chloride	47.61 mg Magnesium chloride
18	8.364 g Magnesium chloride hexahydrate	101.65 mg Magnesium chloride hexahydrate
21	10.138 g Magnesium sulphate	123.24 mg Magnesium sulphate
22	1 g Phosphorus (P) corresponds to	At pH 4.3 1 g Phosphorus (P) corresponds to 32.28 mEq H ₂ PO ₄ ⁻ ions, and 1 mEq H ₂ PO ₄ ⁻ ions corresponds to 30.97 mg phosphorus (with only a small error these figures can be used)
11	5.556 g Calcium phosphate, dibasic	At pH 9.6 1 g Phosphorus (P) corresponds to 64.57 mEq HPO ₄ ²⁻ ions, and 1 mEq HPO ₄ ²⁻ ions corresponds to 15.49 mg phosphorus.
31	4.394 g Potassium phosphate, monobasic	At pH 7.4 and 38 °C 1 g Phosphorus corresponds to 58.1 mEq H ₂ PO ₄ ⁻ ions, and 1 mEq Phosphate ions corresponds to 17.2 mg phosphorus.
32	5.624 g Potassium phosphate, dibasic	20% H ₂ PO ₄ ⁻ ions and ca. 80% HPO ₄ ²⁻ ions).
36	4.455 g Sodium acid phosphate	
37	5.037 g Sodium acid phosphate dihydrate	
46	4.583 g Sodium phosphate	
47	5.746 g Sodium phosphate dihydrate	
48	11.563 g Sodium phosphate dodecahydrate	
23	1 g = 25.57 mEq Potassium (K ⁺) corresponds to	1 mEq = 39.10 mg Potassium (K ⁺) corresponds to
24	2.510 g Potassium acetate	98.15 mg Potassium acetate
25	2.560 g Potassium bicarbonate	100.12 mg Potassium bicarbonate
26	3.044 g Potassium bromide	119.01 mg Potassium bromide
27	1.907 g Potassium chloride	74.56 mg Potassium chloride
28	2.766 g Potassium citrate	108.14 mg Potassium citrate
29	5.991 g Potassium D-gluconate	234.25 mg Potassium D-gluconate
31	3.480 g Potassium phosphate, monobasic	136.09 mg Potassium phosphate, monobasic
32	2.227 g Potassium phosphate, dibasic	87.09 mg Potassium phosphate, dibasic
33	1 g = 43.50 mEq Sodium (Na ⁺) corresponds to	1 mEq = 22.99 mg Sodium (Na ⁺) corresponds to
34	5.919 g Sodium acetate	136.08 mg Sodium acetate
35	5.722 g Sodium acid citrate	131.56 mg Sodium acid citrate
36	6.002 g Sodium acid phosphate	137.99 mg Sodium acid phosphate
37	6.786 g Sodium acid phosphate dihydrate	156.01 mg Sodium acid phosphate dihydrate
38	9.185 g Sodium aminosalicilate	211.15 mg Sodium aminosalicilate
39	3.654 g Sodium bicarbonate	84.01 mg Sodium bicarbonate
41	2.542 g Sodium chloride	58.44 mg Sodium chloride
42	4.264 g Sodium citrate	98.03 mg Sodium citrate
43	5.178 g Sodium citrate	119.05 mg Sodium citrate
44	4.874 g Sodium lactate	112.06 mg Sodium lactate
46	3.087 g Sodium phosphate	70.98 mg Sodium phosphate
47	3.781 g Sodium phosphate dihydrate	88.99 mg Sodium phosphate dihydrate
48	7.789 g Sodium phosphate dodecahydrate	179.07 mg Sodium phosphate dodecahydrate
49	6.964 g Sodium salicylate	160.11 mg Sodium salicylate
50	3.089 g Sodium sulphate (anhydrous)	71.02 mg Sodium sulphate (anhydrous)
51	7.007 g Sodium sulphate	161.10 mg Sodium sulphate
52	3.439 g Sodium thiosulphate	79.05 mg Sodium thiosulphate
53	1 g Sulphur (S) corresponds to	1 g Sulphur (S) corresponds to 62.37 mEq SO ₄ ²⁻ ions and 1 mEq ions corresponds to 16.03 mg sulphur.
12	4.059 g Calcium thiosulphate	At pH 7.4 and 38 °C and with an albumin/globulin ratio of 1.6, serum proteins corresponds to 0.241 basic mEq of ionized serum proteins, and 1 mEq of ionized serum proteins corresponds to 4.1 serum proteins*.
21	7.687 g Magnesium sulphate	
50	4.430 g Sodium sulphate (anhydrous)	
51	10.048 g Sodium sulphate	
52	2.465 g Sodium thiosulphate	

* The conversion factors (0.449 and 2.23) given here for vol% CO₂ into mmol CO₂/l and mEq CO₂/l (bicarbonate-CO₂) are derived from the molar volume of this gas (22.257 l) at 0 °C and 760 mm Hg. The conversion factor 2.24 often used in medical literature is mistakenly based on the molar vol-

ume of ideal gases (22.414 l). For practical purposes the difference between these two factors is negligible.

* From VAN SLYKE et al., *J. Biol. Chem.*, 79, 768 (1928).

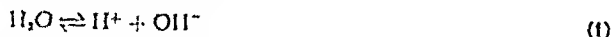
Name	Molecular weight	Hydrogen equivalent	11 of 0.1 N solution contains (gramme)	Mass of log ₁₀ of equivalent weight*
Acetic acid	60.05	$C_2H_3O_2$	6.005	7785
Ammonia	17.03	NH_3	1.703	2312
Ammonium chloride	53.49	NH_4Cl	5.349	7283
Ammonium hydroxide	35.05	NH_4OH	3.505	5447
Ammonium nitrate	80.04	NH_4NO_3	8.004	9033
Ammonium sulphate	132.14	$\frac{1}{2}(NH_4)_2SO_4$	6.607	8200
Ammonium thiocyanate	76.12	NH_4CNS	7.612	8815
Barium carbonate	197.35	$\frac{1}{2}BaCO_3$	9.868	9942
Barium chloride	244.28	$\frac{1}{2}[BaCl_2 + 2H_2O]$	12.214	0869
Barium hydrosulphide	315.48	$\frac{1}{2}[Ba(OH)_2 + 2H_2S]$	15.774	1979
Barium oxide	153.34	$\frac{1}{2}BaO$	7.667	8846
Borax: <i>Ses Sodium tetraborate decahydrate</i>	61.83	$\frac{1}{2}H_2B_4O_7$	2.061	1341
Boric acid	159.81	$\frac{1}{2}B_2O_3$	7.991	9026
Bromine				
Calcium carbonate	100.09	$\frac{1}{2}CaCO_3$	5.005	6994
Calcium chloride	110.99	$\frac{1}{2}CaCl_2$	5.550	7443
Calcium chloride hexahydrate	219.08	$\frac{1}{2}[CaCl_2 + 6H_2O]$	10.954	0396
Calcium hydroxide	74.09	$\frac{1}{2}Ca(OH)_2$	3.705	5668
Calcium oxide	56.08	$\frac{1}{2}CaO$	2.804	4478
Carbon dioxide	44.01	$\frac{1}{2}CO_2$	2.201	3426
Chlorine	70.91	$\frac{1}{2}Cl_2$	3.546	5497
Citric acid	210.14	$\frac{1}{3}[C_6H_8O_7 + 12H_2O]$	7.005	8454
Copper oxide	79.55	$\frac{1}{2}CuO$	3.978	5997
Copper sulphate	249.68	$\frac{1}{2}[CuSO_4 + 5H_2O]$	12.484	0954
Iodic acid	127.91	HI	12.791	1069
Iodobromic acid	80.91	2HBr	8.091	9080
Iydrochloric acid	36.46	HCl	3.646	5618
Ihydrocyanic acid	27.03	HCN	2.703	4318
Iodine	253.81	$\frac{1}{2}I_2$	12.691	1035
Lactic acid	90.08	$C_3H_5O_3$	9.008	9546
Lead carbonate	267.20	$\frac{1}{2}PbCO_3$	13.360	1258
Lead oxide	223.19	$\frac{1}{2}PbO$	11.160	0477
Magnesium carbonate	84.31	$\frac{1}{2}MgCO_3$	4.216	6249
Magnesium chloride	95.21	$\frac{1}{2}MgCl_2$	4.761	6777
Magnesium chloride hexahydrate	203.30	$\frac{1}{2}[MgCl_2 + 6H_2O]$	10.165	1073
Magnesium oxide	40.31	$\frac{1}{2}MgO$	2.016	3044
Malic acid	134.09	$\frac{1}{2}C_4H_6O_5$	6.705	8264
Manganese sulphate	151.00	$\frac{1}{2}MnSO_4$	7.550	9779
Mercuric chloride (corrosive sublimate)	271.50	$\frac{1}{2}HgCl_2$	13.575	1327
Nitric acid	63.01	HNO ₃	6.301	7994
Nitrous acid	47.01	HNO ₂	4.701	6722
Oxalic acid	90.04	$\frac{1}{2}C_2H_2O_4$	4.502	6534
Oxalic acid dihydrate	126.07	$\frac{1}{2}[C_2H_2O_4 + 2H_2O]$	6.304	7996
Phosphoric acid	98.00	$\frac{1}{2}H_3PO_4$	3.267	5141
Potassium bicarbonate	100.12	KHCO ₃	10.012	0005
Potassium bitartrate	188.18	$C_4H_4O_6K$	18.818	2746
Potassium carbonate	138.21	$\frac{1}{2}K_2CO_3$	6.911	8395
Potassium chloride	74.56	KCl	7.456	8725
Potassium cyanide	65.12	KCN	6.512	8137
Potassium dichromate	294.19	$\frac{1}{6}K_2Cr_2O_7$	4.903	6905
Potassium hydroxide	56.11	KOH	5.611	7490
Potassium oxide	94.20	$\frac{1}{2}K_2O$	4.710	6730
Potassium permanganate in acid medium	158.04	$\frac{1}{5}KMnO_4$	3.161	4998
Potassium permanganate for Mn determination	158.04	$\frac{1}{5}KMnO_4$	5.268	7216
Potassium tartrate	226.28	$\frac{1}{2}C_4H_4O_6K_2$	11.314	0536
Potassium tetroxalate	254.20	$\frac{1}{2}[K_2(C_2O_4)_2 + 2H_2O]$	8.473	9280
Silver nitrate	169.87	AgNO ₃	16.987	2301
Sodium bicarbonate	84.01	NaHCO ₃	8.401	9243
Sodium carbonate	105.99	$\frac{1}{2}Na_2CO_3$	5.300	7243
Sodium chloride	58.44	NaCl	5.844	7667
Sodium hydroxide	40.00	NaOH	4.000	6021
Sodium oxide	61.98	$\frac{1}{2}Na_2O$	3.099	4912
Sodium phosphate (disodium phosphate)	177.99	$\frac{1}{2}[Na_2HPO_4 + 2H_2O]$	8.900	9494
Sodium phosphate (trisodium phosphate)	380.12	$\frac{1}{3}[Na_3PO_4 + 12H_2O]$	12.671	1028
Sodium sulphate	78.04	$\frac{1}{2}Na_2SO_4$	3.902	5913
Sodium tetraborate	201.22	$\frac{1}{2}Na_2B_4O_7$	10.061	0026
Sodium tetraborate decahydrate (borax)	381.37	$\frac{1}{2}[Na_2B_4O_7 + 10H_2O]$	19.069	2803
Succinic acid	118.09	$\frac{1}{2}C_4H_6O_4$	5.905	7712
Sulphuric acid	98.08	$\frac{1}{2}H_2SO_4$	4.904	6906
Sulphur trioxide	80.06	$\frac{1}{2}SO_3$	4.003	6024
Tartaric acid	150.09	$\frac{1}{2}C_4H_4O_6$	7.505	8754
Zinc sulphate	287.54	$\frac{1}{2}[ZnSO_4 + 7H_2O]$	14.377	1577

* For logarithms see page 10

Definitions of pH scales^{1,2}

A. Dissociation constant of water

The relationship between the concentrations of hydrogen ions* and hydroxyl ions in an aqueous medium is fixed by the dissociation equilibrium of water:



If solutes are present in such small concentrations that the activity of water is practically unity**, the ion product constant*** of water is given by

$$K_w = a_{\text{H}^+} a_{\text{OH}^-} = m_{\text{H}^+} \gamma_{\text{H}^+} m_{\text{OH}^-} \gamma_{\text{OH}^-} \quad (2)$$

where a = ionic activity, γ = activity coefficient, m = molality.

The dissociation of pure water is extremely small***, and if no solutes are present

$$\gamma_{\text{H}^+} \gamma_{\text{OH}^-} \approx 1 \quad (3)$$

Since the value of K_w at 25 °C is 1.008×10^{-14} it follows that for pure water

$$m_{\text{H}^+} = m_{\text{OH}^-} = \sqrt{K_w} \approx 1 \times 10^{-7} \quad (4)$$

In water the molality ϵ of the ions is practically identical with the molality m (see page 271), so that for pure water

$$\epsilon_{\text{H}^+} \approx m_{\text{H}^+} \approx 1 \times 10^{-7} \quad (5)$$

In aqueous solutions the solutes may give rise to additional H^+ ions (dissociation of acids, hydrolysis of salts, etc.), with the result that the equilibrium (1) is displaced and the concentration of OH^- ions reduced. In the same way additional OH^- ions cause a decrease in the concentration of H^+ ions, so that $\epsilon_{\text{H}^+} \ll 1 \times 10^{-7}$. In the former case the solution is said to be 'acid', in the latter 'alkaline'. Since the ion product constant K_w is markedly temperature-dependent the same applies to the neutral point of ϵ_{H^+} , the value of which at 0 °C is $1 \times 10^{-7.4}$, at 60 °C $1 \times 10^{-6.6}$.

Temperature dependence of the ion product constant of water (K_w)²

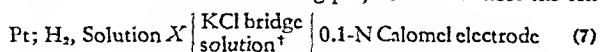
°C	$K_w \times 10^{14}$	$-\log K_w$	°C	$K_w \times 10^{14}$	$-\log K_w$
0	0.1139	14.943	35	2.089	13.680
5	0.1846	14.734	40	2.919	13.535
10	0.2920	14.535	45	4.018	13.396
15	0.4505	14.346	50	5.474	13.262
20	0.6809	14.167	55	7.297	13.137
25	1.008	13.996	60	9.614	13.017
30	1.469	13.833			

3. The SORENSEN pH scale

SOESEN was the first to realize the importance of hydrogen ion concentration in biochemical processes, and he devised colorimetric and potentiometric methods of measuring quantities which in the light of the thermodynamic concepts of the time (1909) were considered as strictly equal to the molality of the hydrogen ion. At the same time he introduced the abbreviation now written as pH:

$$\text{pH} = -\log_{10} \epsilon_{\text{H}^+} \quad (6)$$

As the actual means of measuring pH, SOESEN chose the cell



* For the sake of simplicity the expressions hydrogen ion and hydroxyl ion are here used, although these ions never occur in the free state but only associated with water molecules (mainly in the form of H_3O^+ and H_2O^-).

** The activity of water in an aqueous solution is p/p° , where p and p° are the pressures of water vapour in equilibrium respectively with the solution and with pure water at the temperature in question, provided that p and p° are so small that water vapour can be considered an ideal gas.

*** The dissociation constant of water, rarely to be found in the literature, given by $K_w/m_{\text{H}_2\text{O}}$, the value of $m_{\text{H}_2\text{O}}$ being 55.51.

† The KCl solution is usually contained in a tube connecting the two halves of the cell and prevented from mixing with the other two solutions by means of agar plugs. Diffusion potentials arise at the two liquid junctions but these are of opposite sign and almost equal because of the similar transference numbers of the K^+ and Cl^- ions. SOESEN originally attempted to measure E at various concentrations of the KCl bridge and to extrapolate to a zero fusion potential. Under the present convention, the KCl bridge must have a constant concentration of 3.5-N saturated KCl is 4.2-N maintained con-

the e.m.f. of which (E) is compared with that (E') of a similar cell containing a solution^{††} of $\epsilon_{\text{H}^+} = 1$ in place of the solution. This purpose the hydrogen electrode could be replaced by other electrode responsive to H^+ ions (a quinhydrone or a glass electrode for instance). Other reference electrodes could likewise be used in place of the calomel electrode. It is necessary only that the comparison be made under the same conditions, such as constancy of temperature. According to SOESEN, the pH of the solution X is given by

$$\text{pH}_{\text{SOESEN}} = \frac{(E - E')F}{RT \ln 10}$$

where F is the FARADAY constant, R the molar gas constant, absolute temperature, and $\ln 10 = 2.30259$. Values of $(RT \ln 10)$ at various temperatures are given on the opposite page.

C. The conventional pH scale

It is now known that the e.m.f. of the cell (7) is dependent not only on the concentration of H^+ ions but also on their activity, the activity of the Cl^- ions, and on the transference numbers of the ions (variation of the diffusion potential with ionic concentration). For this reason comparison is no longer made with a reference solution whose ϵ_{H^+} value is assumed to be unity but with a standard solution S whose pH value (pH_S) is fixed by convention. The value of the solution X is then defined conventionally as

$$\text{pH}_X = \frac{(E_X - E_S)F}{RT \ln 10} + \text{pH}_S$$

In the United Kingdom⁴ and Japan⁵ the primary standard solution is 1/20-molar potassium hydrogen phthalate, while in the USA⁶ five standard solutions are in use (all these standards follow the same conventions). The five US standard solutions have assigned pH_S values between 3.5 and 9.5. This allows of an alternative definition of pH through comparison of the solution X with two standards S and S' , when pH_X is obtained from the following formula:

$$\frac{\text{pH}_X - \text{pH}_S}{\text{pH}_{S'} - \text{pH}_S} = \frac{E - E_S}{E_{S'} - E_S}$$

This procedure is especially recommended when the H^+ -responsive electrode is a glass electrode. Differences in measured values of pH obtained by the use of different standard solutions are too small to be of practical significance.

Values of pH on the SOESEN and conventional scales differ by a constant amount as follows²:

$$\text{pH} = \text{pH}_{\text{SOESEN}} + 0.04$$

D. Thermodynamic interpretation of the conventional pH scale

It is clear from the above that there exists no definite relationship between the conventional pH scale and any true thermodynamic measurement of the acidity of a solution such as H^+ molality (m_{H^+}). This scale meets all practical needs, however, and there is little value in introducing more complicated means of measurement for the sake of thermodynamic principles. The difficulty lies in the fact that while only the product $\gamma_{\text{H}^+} \gamma_{\text{Cl}^-}$ activity coefficients of the cation and anion has any clear thermodynamic meaning, this is a quantity which cannot be measured by means of arrangements like the cell (7). The difficulty has been overcome by defining the activity of the chloride ion by

$$\log \gamma_{\text{Cl}^-} = - \frac{A\sqrt{I}}{1 + B'\sqrt{I}}$$

where A is the DEBYE-HÜCKEL constant⁷ = 1.82×10^6 (where ϵ = dielectric constant of the solution), B' a constant depending on the finite size of the ion, and I the ionic strength (not exceeding 0.1) defined as $\frac{1}{2} \sum m_i z_i^2$ for all the ionic species present. On the basis of this equation it can be assumed that for solutions of ionic strength less than 0.1 and pH values between 2 and 12

$$\text{pH} = -\log (m_{\text{H}^+} \gamma_{\text{H}^+}) = -\log a_{\text{H}^+}$$

†† SOESEN used HCl with a constant concentration of 0.1-N.

es of $(RT \ln 10)/F$ from 0° to 100°C*2

°C	$RT \ln 10/F$	°C	$RT \ln 10/F$
0	0.054197	50	0.064118
5	0.055189	55	0.065110
10	0.056181	60	0.066102
15	0.057173	65	0.067094
20	0.058165	70	0.068086
25	0.059157	75	0.069078
30	0.060149	80	0.070070
35	0.061141	85	0.071062
38	0.061737	90	0.072054
40	0.062133	95	0.073046
45	0.063126	100	0.074038

$\ln 10 = 2.30259$, $R = 8.3143 \text{ J mol}^{-1} \text{ deg}^{-1}$, $F = 96487 \text{ C mol}^{-1}$,
*°C + 273.15.

values of standard solutions at 25°C on different scales*

Solution	Scale of		
	Hitchcock and TAYLOR	MacInnes et al	National Bureau of Standards
Potassium bitartrate, 0.03-molar	3.567	-	3.569
Potassium biphthalate, 0.05-molar	4.010	4.000	4.008
Acetic acid 0.1-molar, Sodium acetate 0.1-molar.	4.645	4.640	4.652
KH_2PO_4 0.025-molar, NaH_2PO_4 0.025-molar	6.855	-	6.865
Sodium tetraborate decahydrate 0.05-molar (borax)	9.180	-	9.196

1.2 values of NBS primary standards from 0° to 95°C*

Temperature (°C)	Potassium bitartrate (saturated at 25°C)	Potassium biphthalate 0.05-molar	KH_2PO_4 0.025-molar, NaH_2PO_4 0.025-molar	KH_2PO_4 0.00805-molar, NaH_2PO_4 0.02043-molar	Sodium tetraborate decahydrate (borax) 0.05-molar
0	-	4.003	6.984	7.534	9.464
5	-	3.999	6.951	7.500	9.395
10	-	3.998	6.923	7.472	9.332
15	-	3.999	6.900	7.448	9.276
20	-	4.002	6.881	7.429	9.225
25	3.557	4.008	6.865	7.413	9.180
30	3.552	4.015	6.853	7.400	9.139
35	3.549	4.024	6.844	7.389	9.102
38	3.548	4.030	6.840	7.384	9.081
40	3.547	4.035	6.838	7.380	9.068
45	3.547	4.047	6.834	7.373	9.038
50	3.542	4.060	6.833	7.367	9.011
55	3.554	4.073	6.834	-	8.985
60	3.560	4.091	6.836	-	8.962
70	3.580	4.126	6.843	-	8.921
80	3.609	4.164	6.859	-	8.885
90	3.650	4.205	6.877	-	8.850
95	3.674	4.227	6.886	-	8.833

pH values of secondary British standards*

Solution	12°C	25°C	38°C
Potassium tetroxalate 0.1-molar .	-	1.48	1.50
HCl 0.01-molar, KCl 0.09-molar.	-	2.07	2.08
Acetic acid 0.1-molar, Sodium acetate 0.1-molar	4.65	4.64	4.65
Acetic acid 0.01-molar, Sodium acetate 0.01-molar	4.71	4.70	4.72
KH_2PO_4 0.025-molar, Na_2HPO_4 0.025-molar	-	6.85	6.84
Sodium tetraborate decahydrate (borax) 0.05-molar	-	9.18	9.07
NaHCO_3 0.025-molar, Na_2CO_3 0.025-molar	-	10.00	-

Approximate pH values of common reagent solutions at or near room temperature*

Solution	Molarity	pH
Ammonia water	0.1	11.3
Ammonium chloride	0.1	4.6
Ammonium dihydrogen phosphate .	0.1	4.0
Ammonium oxalate	0.1	6.4
Ammonium sulphate	0.1	5.5
Barbital sodium	0.1	9.4
Benzoic acid	saturated	2.8
Boric acid	0.1	5.3
Calcium hydroxide	saturated	12.4
Citric acid	0.1	2.1
Diammonium hydrogen phosphate	0.1	7.9
Sodium hydrogen phosphate . . .	0.1	9.2
Hydrochloric acid	0.1	1.1
Oxalic acid	0.1	1.3
Potassium acetate	0.1	9.7
Potassium aluminum sulphate . .	0.1	4.2
Potassium bicarbonate	0.1	8.2
Potassium carbonate	0.1	11.5
Potassium dihydrogen phosphate .	0.1	4.5
Salicylic acid	saturated	2.4
Sodium acetate	0.1	8.9
Sodium benzoate	0.1	8.0
Sodium bicarbonate	0.1	8.3
Sodium bisulphate	0.1	1.4
Sodium carbonate	0.1	11.5
Sodium dihydrogen phosphate . .	0.1	4.5
Sodium hydroxide	0.1	12.9
Sodium tetraborate decahydrate .	0.1	9.4
Succinic acid	0.1	2.7
Tartaric acid	0.1	2.0
Trichloroacetic acid	0.1	1.2

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Buffer solutions (or buffers) are solutions whose pH value is to a large degree insensitive to the addition of other substances. It is important to realize, however, that the pH value of a buffer solution does not change only when acids or bases are added or on dilution but also when the temperature changes or neutral salts are added. In accurate work therefore, it is important to check the pH value electrometrically after all the ingredients have been added. The extent to which the pH values of buffer solutions vary when acids or bases are added or the temperature changes is shown in the tables which follow. In general, dilution to half the concentration changes the pH value by only some hundredths of a unit (Buffer No. 1 in the table is an exception in that the change amounts to ca. pH 0.15); addition of 0.1-molar neutral salt solution may change the pH value by ca. 0.1.

In the table opposite the solutions are classified into general buffers (mostly in use for the last 50 years), universal buffers with a low buffering capacity but a wide pH range, and buffers for biological

media with a moderate pH range but containing stable ingredients (phosphate and borate, for example, often undergo side reactions with biological media). An important property is often the transparency to ultraviolet light. Occasionally it is desirable to have a volatile buffer which can be readily removed¹ (examples are buffers Nos. 20 and 21) but the use of very volatile systems makes a control of the pH essential. Most of the pH data to be found in literature relate to the SORESENSEN scale, and it should be noted that the values given in the following table of buffers are on the conventional pH scale (cf. 'pH Standards', page 278).

Both stock and buffer solutions should be made up with distilled water free of CO₂. Only standard reagents should be used. If there is any doubt as to the purity or water content of solutions the molarity must be checked by titration. The amounts x of stock solutions required to make up a buffer solution of the desired pH value are given in the table on page 282.

Reference

¹ For a list of volatile buffers see MICHL, H., in HEFTMANN, E. (Ed.), *Chromatography*, part 1, Reinhold, New York, 1961, page 250.

* This section (pages 280-282) has been compiled by F. KOHLER, Department of Physical Chemistry, University of Vienna.

No.	Name	pH range	Temperature	pH change per °C
<i>General buffers</i>				
1	KCl/HCl (CLARK and LUNS) ¹	1.0- 2.2	Room	0
2	Glycine/HCl (SORENSEN) ²	1.2- 3.4	Room	0
3	Na citrate/HCl (SORENSEN) ²	1.2- 5.0	Room	0
4	K biphthalate/HCl (CLARK and LUNS) ¹	2.4- 4.0	20 °C	+ 0.001
5	K biphthalate/NaOH (CLARK and LUNS) ¹	4.2- 6.2	20 °C	
6	Na citrate/NaOH (SORENSEN) ²	5.2- 6.6	20 °C	+ 0.004
7	Phosphate (SORENSEN) ²	5.0- 8.0	20 °C	- 0.003
8	Barbital-Na/HCl (MICHAELIS) ³	7.0- 9.0	18 °C	
9	Na borate/HCl (SORENSEN) ²	7.8- 9.2	20 °C	- 0.005
10	Glycine/NaOH (SORENSEN) ²	8.6-12.8	20 °C	- 0.025
11	Na borate/NaOH (SORENSEN) ²	9.4-10.6	20 °C	- 0.01
<i>Universal buffers</i>				
12	Citric acid/phosphate (McILVAINE) ⁴	2.2- 7.8	21 °C	
13	Citrate-phosphate-borate/HCl (TEORELL and STENHAGEN) ⁵	2.0-12.0	20 °C	
14	BRITTON-ROBINSON ⁶	2.6-11.8	25 °C	at low pH 0 at high pH -0.02
<i>Buffers for biological media</i>				
15	Acetate (WALPOLE) ⁷⁻⁹	3.8- 5.6	25 °C	
16	Dimethylglutaric acid/NaOH ¹⁰	3.2- 7.6	21 °C	
17	Piperazine/HCl ^{11, 12}	4.6- 6.4 8.8-10.6	20 °C	
18	Tetrathylethylenediamine* ¹²	5.0- 6.8 8.2-10.0	20 °C	
19	Trismaleate ^{7, 13}	5.2- 8.6	23 °C	
20	Dimethylaminoethylamine* ¹²	5.6- 7.4 8.6-10.4	20 °C	
21	Imidazole/HCl ¹⁴	6.2- 7.8	25 °C	
22	Triethanolamine/HCl ¹⁵	7.0- 8.8	25 °C	
23	N-Dimethylaminoleucylglycine/NaOH ¹⁶	7.0- 8.8	23 °C	- 0.015
24	Tris/HCl ⁷	7.2- 9.0	23 °C	- 0.02
25	2-Amino-2-methylpropane-1,3-diol/HCl ^{7, 17}	7.8-10.0	23 °C	
26	Carbonate (DELOREY and KING) ^{7, 17}	9.2-10.8	20 °C	

* Can be combined with tris buffer to give a cationic universal buffer (cf. SEMENZA et al.¹²).

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are not otherwise specified, both stock and buffer solutions should be made up with distilled water free of CO_2 . Only standard reagents should be used. If there is any doubt as to the purity or water content of solutions their molarity must be checked by titration. The amounts x of stock solutions required to make up a buffer solution of the desired pH value are given in the table on page 282.

Buffer No.	Stock solutions		Composition of the buffer
	A	B	
1	KCl 0.2-N (14.91 g/l)	HCl 0.2-N	25 ml A + x ml B made up to 100 ml
2	Glycine 0.1-molar in NaCl 0.1-N (7.507 g glycine + 5.844 g NaCl/l)	HCl 0.1-N	x ml A + (100- x) ml B
3	Disodium citrate 0.1-molar (21.01 g $\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ + 200 ml NaOH 1-N per litre)	HCl 0.1-N	x ml A + (100- x) ml B
4	Potassium biphthalate 0.1-molar (20.42 g $\text{KHC}_8\text{H}_4\text{O}_4$ /l)	HCl 0.1-N	50 ml A + x ml B made up to 100 ml
5	As No. 4	NaOH 0.1-N	50 ml A + x ml B made up to 100 ml
6	As No. 3	NaOH 0.1-N	x ml A + (100- x) ml B
7	Monopotassium phosphate $1/10$ -molar (9.073 g KH_2PO_4 /l)	Disodium phosphate $1/10$ -molar (11.87 g $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ /l)	x ml A + (100- x) ml B
8	Barbital sodium 0.1-molar (20.62 g/l)	HCl 0.1-N	x ml A + (100- x) ml B
9	Boric acid, half-neutralized, 0.2-molar (corr. to 0.05-molar borax, 12.37 g boric acid + 100 ml NaOH 1-N per litre)	HCl 0.1-N	x ml A + (100- x) ml B
10	As No. 2	NaOH 0.1-N	x ml A + (100- x) ml B
11	As No. 9	NaOH 0.1-N	x ml A + (100- x) ml B
12	Citric acid 0.1-molar (21.01 g $\text{C}_6\text{H}_5\text{O}_7 \cdot \text{H}_2\text{O}$ /l)	Disodium phosphate 0.2-molar (35.60 g $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ /l)	x ml A + (100- x) ml B
13	To citric acid and phosphonic acid solutions (ca. 100 ml), each equivalent to 100 ml NaOH 1-N, add 3.54 g cryst. orthoboric acid and 343 ml NaOH 1-N, and make up the mixture to 1 l	HCl 0.1-N	20 ml A + x ml B made up to 100 ml
14	Citric acid, monopotassium phosphate, barbital, boric acid, all 0.02857-molar (6.004 g $\text{C}_6\text{H}_5\text{O}_7 \cdot \text{H}_2\text{O}$, 3.888 g KH_2PO_4 , 5.263 g barbital, 1.767 g H_3BO_3 /l)	NaOH 0.2-N	100 ml A + x ml B
15	Sodium acetate 0.1-N (8.204 g $\text{C}_2\text{H}_3\text{O}_2\text{Na}$ or 13.61 g $\text{C}_2\text{H}_3\text{O}_2\text{Na} \cdot 3\text{H}_2\text{O}$ /l)	Acetic acid 0.1-N (6.005 g/l)	x ml A + (100- x) ml B
16	β -Dimethylglutaric acid 0.1-molar (16.02 g/l)	NaOH 0.2-N	(a) 100 ml A + x ml B made up to 1000 ml (b) 100 ml A + x ml B + 5.844 g NaCl made up to 1000 ml (NaCl Δ 0.1-molar)
17	Piperazine 1-molar (86.14 g/l)	HCl 0.1-N	5 ml A + x ml B made up to 100 ml
18	Tetraethylethylenediamine 1-molar (172.32 g/l)	HCl 0.1-N	5 ml A + x ml B made up to 100 ml
19	Tris acid maleate 0.2-molar (24.23 g tris(hydroxymethyl)aminomethane + 23.21 g maleic acid or 19.61 g maleic anhydride/l)	NaOH 0.2-N	25 ml A + x ml B made up to 100 ml
20	Dimethylaminoethylamine 1-molar (88 g/l)	HCl 0.1-N	5 ml A + x ml B made up to 100 ml
21	Imidazole 0.2-molar (13.62 g/l)	HCl 0.1-N	25 ml A + x ml B made up to 100 ml
22	Triethanolamine 0.5-molar (76.11 g/l) containing 20 g/l ethylenediaminetetra-acetic acid disodium salt ($\text{C}_{10}\text{H}_{16}\text{O}_8\text{N}_4\text{Na}_4 \cdot 2\text{H}_2\text{O}$)	HCl 0.05-N	10 ml A + x ml B made up to 100 ml
23	<i>N</i> -Dimethylaminooleucylglycine 0.1-molar (24.33 g $\text{C}_{20}\text{H}_{33}\text{O}_5\text{N}_2 \cdot 1/2\text{H}_2\text{O}$ /l) containing NaCl 0.2-N (11.69 g/l)	NaOH 1-N 100 ml made up to 1 l with A	x ml A + (100- x) ml B

Buffer Solutions

The table gives the amounts (x ml) of the stock solutions listed on page 281 required to make up a buffer solution of the desired pH value

[illegible]

Indicator	Acid side	pH range	Alkaline side
Cresol red, 1st range	red	0.2- 1.8	yellow
<i>m</i> -Cresol purple, 1st range	red	1.2- 2.8	yellow
Thymol blue, 1st range	red	1.2- 2.8	yellow
Metanil yellow	red	1.2- 2.3	yellow
Tropaeolin 00 (orange IV)	red	1.4- 3.2	yellow
2,6-Dinitrophenol	colourless	1.7- 4.4	yellow
Benzyl orange	red	1.9- 3.3	yellow
2,4-Dinitrophenol	colourless	2.0- 4.7	yellow
<i>p</i> -Dimethylaminoazobenzene	red	2.9- 4.0	yellow
Bromophenol blue	yellow	3.0- 4.6	violet
Congo red	blue	3.0- 5.0	red
Bromochlorophenol blue	yellow	3.0- 4.6	purple
Methyl orange	red	3.1- 4.4	yellow
Bromocresol green	yellow	3.8- 5.4	blue
2,5-Dinitrophenol	colourless	4.0- 5.8	yellow
Methyl red	red	4.2- 6.3	yellow
Azolitmin (litmus)	red	4.4- 6.6	blue
Propyl red	red	4.6- 6.6	yellow
<i>p</i> -Nitrophenol	colourless	4.7- 7.9	yellow
Bromocresol purple	yellow	4.8- 6.8	purple
Bromophenol red	yellow	4.8- 6.8	purple
Chlorophenol red	yellow	5.0- 6.9	purple
Bromothymol blue	yellow	6.0- 7.6	blue
<i>m</i> -Nitrophenol	colourless	6.6- 8.6	yellow
Neutral red	red	6.8- 8.0	yellow
Phenol red	yellow	6.8- 8.4	red
Rosolic acid	brown	6.9- 8.0	red
Cresol red, 2nd range	yellow	7.2- 8.8	purple
α -Naphtholphthalein	brown	7.3- 8.7	green
Orange I (Tropaeolin 000 No 1)	yellow	7.6- 8.9	rose
<i>m</i> -Cresol purple, 2nd range	yellow	7.6- 9.2	purple
Thymol blue, 2nd range	yellow	8.0- 9.6	blue
<i>m</i> -Cresolphthalein	colourless	8.2- 9.8	red
Phenolphthalein	colourless	8.3-10.0	red
Thymolphthalein	colourless	9.3-10.5	blue
β -Naphthol violet	yellow	10.0-12.0	violet
Alizarin yellow R	yellow	10.0-12.1	brown
Alizarin yellow GG	yellow	10.0-12.0	orange
Nitramine	colourless	10.8-13.0	brown
Poirrier blue	blue	11.0-13.0	red
Tropaeolin 0 (resorcin yellow)	yellow	11.1-12.7	orange

Many of the spectral emission lines listed in the tables below are readily detectable only in the hotter flames such as oxy-hydrogen or oxy-acetylene and in some cases only in the inner cone.

For further data on flame photometry see the literature¹.

Flame lines and bands of analytical importance²

The emissions are arranged in order of wave length. Inclusion does not necessarily mean that the emission is suitable for quantitative measurement of the element concerned. Band emissions are given at the most sensitive wave length and are marked 'b'.

Wave length (nm)	Element	Wave length (nm)	Element	Wave length (nm)	Element
228.8	Cd	375.8	Fe	495 b	B
253.7	Hg	377.6	Tl	497 b	Ti
285.2	Mg	378.6	Ru	500 b	Zn
303.4	Sn	383 b	Mg	510 b	Be
307.6	Zn	385.6	Fe	518 b	Ti
317.5	Sn	386.0	Fe	520.5	Cr
324.8	Cu	387.3	Co	520.6	Cr
326.1	Cd	387.4	Co	520.8	Cr
327.4	Cu	396.2	Al	521 b	B
328.1	Ag	403.3	Ga	535.0	Tl
330.2	Na	403.5	Mn	540 b	Mo
330.3	Na	404.4	K	548 b	B
338.3	Ag	404.7	K	550 b	U
340.5	Pd	405.8	Pb	552 b	Dy
341.2	Co	407.8	Sr	553.6	Ba
341.5	Ni	410.2	In	554 b	Ca
343.5	Rh	417.2	Ga	560 b	La
344.6	K	420.2	Rb	562 b	Pr
344.7	K	421.6	Sr	565 b	Tb
349 b	Sn	422.7	Ca	570 b	Gd
350.2	Co	425.4	Cr	570 b	Dy
350.3	Rh	427.5	Cr	571 b	Pr
351.5	Ni	429.0	Cr	576 b	V
352.4	Ni	430.4	Nd	589.0	Na
352.5	Ni	438 b	La	589.5	Na
353.0	Co	442 b	La	600 b	Mo
360.5	Cr	444 b	Y	600 b	Tb
361.0	Pd	450 b	Nb	622 b	Ca
363.5	Pd	450 b	Gd	653 b	Sm
364 b	Te	451.1	In	660 b	Nd
368.4	Pb	455.4	Ba	670.8	Li
369.2	Rh	455.5	Cs	681 b	Sr
371 b	Mg	460.7	Sr	715 b	Ti
372 b	Te	460.9	Sc	766.5	K
372.0	Fe	462 b	Gd	769.9	K
372.3	Fe	462 b	Nb	780.0	Rb
372.8	Ru	466.2	Eu	794.8	Rb
373.3	Fe	467 b	Al	818.3	Na
373.5	Fe	471 b	Be	819.5	Na
373.7	Fe	472.3	Bi	852.1	Cs
374.3	Fe	481 b	Ce	873 b	Ba
374.6	Fe	483 b	Y	894.3	Cs
374.8	Fe	484 b	Al		
374.9	Fe	493.4	Ba		

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- ² From MACINTYRE, I., in LONG, C. (Ed.), *Biochemists' Handbook*, Spon, don, 1961, page 10. Reproduced by kind permission of the author and publishers.

Detailed flame spectra of sodium, potassium, calcium and magnesium²

The ionization potential of the neutral atom and excitation potential of singly ionized atom (expressed in eV) are given in brackets. 'r' represents transition to ground state. The most suitable wave lengths for analysis are given in *italics*. 'I' signifies the neutral atom, 'II' the singly ionized atom.

Element	Wave length (nm)	Emitter	Excitation potential (eV)
Na (5.14; 33.3)	285.3 r	I	4.06
	330.2 r	I	3.75
	330.3 r	I	3.75
	568.3	I	4.03
	568.8	I	4.03
	589.0 r	I	2.10
	589.5 r	I	2.10
	818.3	I	3.61
K (4.34; 20.6)	819.5	I	3.61
	344.6 r	I	3.59
	344.7 r	I	3.59
	404.4 r	I	3.06
	404.7 r	I	3.06
	693.9	I	3.40
	696.4	I	3.40
	766.5 r	I	1.61
Ca (6.11; 3.12)	769.9 r	I	1.61
	422.7 r	I	2.93
	393.4 r	II	3.15
	396.8 r	II	3.12
	622	CaO	1.97
Mg (7.64; 4.42)	554	CaO	1.97
	277.7	I	7.17
	277.8	I	7.17
	278.0	I	7.17
	278.1	I	7.17
	278.3	I	7.17
	285.2 r	I	4.34
	333.0	I	6.43
	333.2	I	6.43
	333.7	I	6.43
	382.9	I	5.85
	382.2	I	5.85
	383.8	I	5.85
	279.6 r	II	4.43
	280.3 r	II	4.42
	371	MgO	3.49
	383	MgO	3.35

capac from the atom, giving rise to a slow, positively charged ion and a very fast secondary electron. If the ions and electrons are not immediately separated by means of an electric field they recombine and remain undetected. Electrons slowed by multiple collisions can be captured by reactive gas molecules and give rise to negative ions. Furthermore, an ion strongly accelerated in an electric field may collide with a neutral gas molecule and thereby give rise to a fresh positive ion and electron (see GRIGER counters, below). X and γ -rays must also first give rise to free electrons before they can be detected, and since the probability of ionization occurring decreases rapidly with increasing quantum energy, the harder such radiation is, the more difficult it is to detect.

Ionization chambers. While ionization chamber measurements form the absolute basis of dosimetry (see below), the method is too slow and insensitive for detecting short-lived radioactivity in the μCi range and lower.

Geiger counters. These are gas-filled counters operating at reduced pressure. They do not measure continuous currents like ionization chambers but register collision ionizations. The primary ions in the counter gas are multiplied by applying an electric field of 800–2000 V (ion 'avalanche'). In the range of roughly 200–600 V the number of ions present is strictly proportional to the number of primary ions (proportional region), and for this reason proportional counters can be used to distinguish β -rays from highly ionizing particles. At higher voltages (> 800 V) a 'plateau' region is reached in which the ion avalanche is largely independent of the intensity of primary ionization. The life-time of a gas-filled counter is limited by the capacity of the gas to a total of 10^9 – 10^{10} collision discharges; for halogen-filled tubes it is about 10^{12} . During a collision ionization, which lasts about 0.1 ms, the counter is refractory to additional ionizations (counter dead time). In the plateau region the resolving time – or minimum time between two counted discharges – is about 0.2 ms, in the proportional region about 1 μs .

Semiconductor detectors. When silicon or germanium crystals are irradiated, ionization occurs and secondary electrons are released. With the aid of electron donors (for example lithium) these can be conducted to electrodes and measured as current pulses. Such drift detectors are suitable for detecting corpuscular and low-energy X and γ -rays at room temperature. On account of their extremely small size they can even be implanted.

Scintillation

This is the name given to the light flashes emitted by luminescent substances when excited by high-energy radiation. The flashes can in turn liberate photoelectrons from photosensitive substances (for instance caesium/antimony phosphors); the photoelectrons are amplified 10^7 – 10^8 times by means of a phototube multiplier before being converted into current pulses. The pulse height depends on the energy of the original γ - or corpuscular radiation, and the pulses can thus be sorted by means of a discriminator (pulse height analyser). By using different discriminator channels the different nuclides in a mixture of isotopes can be determined either successively or simultaneously.

Solid scintillators. The commonest type in use in nuclear medicine consists of single crystals of thallium-activated sodium iodide. Since the decay time of the fluorescence is only 0.25 μs the scintillation crystals have a resolving power about a thousand times greater than gas-filled counters. Moreover, the pulse yield for X and γ -rays is 10–1000 times greater – depending on the crystal volume and surface – as a result of the higher density of the material. Since there is no dissipation of the crystals the life-time of these scintillation detectors is limited only by that of the replaceable multiplier and its semi-permanent photosensitive layer. The wave length of the luminescent radiation is about 410 nm. Organic scintillators and plastic scintillators have a decay time of 5–24 ns, their secondary luminescence a wave length of 410–440 nm.

Liquid scintillators. The radiation from preparations emitting β -rays, soft X-rays or γ -rays can be measured with particularly high pulse yield if they are mixed directly with a scintillator solution.

Only a few highly purified alkylbenzenes (mainly toluene and xylene) and ethers (anisole, veratrole, dioxan) are suitable as solvents. They transmit the radiation energy to the scintillators by ionization via metastable (10^{-12} – 10^{-9} s) excited states. This type of energy transmission is subject to interference by fluorescence quenching.

The 'first' scintillator usually consists of a solution of 2,5-diphenyloxazole (PPO) in toluene (4 g/l). Its fluorescence, which is highly subject to quenching, has a maximum at 380 nm. Since the photocathodes of many multipliers develop optimum activity only at wave lengths above 400 nm the spectrum of the primary fluorescence must be displaced to higher wave lengths by using a second

fluorescent substance. Other suitable first scintillators are 2,5-(4-diphenyl)-1,3,4-oxadiazole (PBD or PBO) (in toluene, 360 nm) and *p*-terphenyl (8 g/l; 350 nm). 2,5-Bis-(2-[5-*tert*. benzoxazolyl])thiophen (BBO-T) emits light at 435 nm and fore needs no second scintillator.

The 'second' scintillator converts the ultraviolet radiation first by fluorescence into radiation with a wave length of 420 nm. It usually consists of 1,4-di-(2-[5-phenyloxazolyl])benzene (POPOP) in toluene at a concentration of 0.1–2.0 g/l. A sm of the fluorescence of this substance is due to primary radio and reduces quenching in the first scintillator.

If the radioactive preparation in question is insoluble in solvent, other substances must be added to make it soluble. Like however, these substances considerably reduce the pulse yield fluorescence quenching. Since the latter also causes spectral placement, however, it can be detected and corrected by discriminatory measurements in two channels or by comparison with an external standard radiator.

Autoradiography

The oldest method of detecting radioactivity is the photographic. Both electromagnetic and corpuscular radiation cause electrons to be expelled from the halogen atoms in the silver halide grain of a gelatin emulsion. Each electron reduces a silver ion (Ag^+) to metallic silver. The sites at which this occurs in the silver grains constitute 'development centres' where the developer brings about the reduction of the whole grain to black metallic silver. The resulting degree of intensification is about 10^{12} .

Macroscopic autoradiography is used in nuclear medicine mainly for radiation exposure monitors (film badges); another use is the localization of radioactivity in chromatograms and in sections of large surface area. The film used is high-sensitivity X-ray film; for pure γ -ray sources an intensifying screen is usually necessary, though this reduces the sharpness of the image. Image intensity is dependent on a great many factors, so that the exposure time must be decided empirically in each case. As an example, an autoradiograph taken by a ^{131}I isotope with a radioactivity of 10 nCi requires an exposure time of 2–4 days.

Microscopic autoradiography of sections 5–10 μm thick requires an activity concentration in the tissue of about 10 $\mu\text{Ci/ml}$ (assuming uniform distribution) if satisfactory blackening of films is to be obtained in 2–16 days. In the case of weakly radioactive sources self-exposure times longer than three times the half-life are possible. The activity of weak β -emitters (^3H , ^{14}C , ^{35}S) can be determined semiquantitatively by counting the blackened grains.

Dosimetry of incorporated nuclides (see also pages 218–221)

If a β -emitter is uniformly distributed throughout an organ or the whole body, and if the range of its β -rays is small compared with the volume of matter concerned, then the absorbed dose D_∞ for complete disintegration is given by

$$D_\infty = K_\beta \times \alpha_0 \times \frac{T_{\text{eff}}}{T_{1/2}} \quad [\text{rd}]$$

where α_0 is the initial activity concentration A_0/m (in $\mu\text{Ci/g}$), $T_{1/2}$ the effective half-life (in days), $T_{1/2}$ the physical half-life (in days), K_β a characteristic constant for each β -emitter (see the table on pages 292 and 293). K_β is given by

$$K_\beta = 73.9 \times E_\beta \times T_{1/2} \quad [\text{rd g } \mu\text{Ci}^{-1}]$$

where $T_{1/2}$ is in days and E_β is the mean energy in MeV of the emission ($\approx 0.3 E_{\text{max}}$; see the table on pages 292 and 293).

The hourly absorbed dose rate after the lapse of a time t from incorporation is given by

$$\dot{D}_\beta = 0.0288 \times K_\beta \times \alpha_0 \times \frac{1}{T_{1/2}} \times e^{-0.693 \frac{t}{T_{\text{eff}}}} \quad [\text{rd h}^{-1}]$$

where $T_{1/2}$ is in days, t and T_{eff} in any time unit provided it is the same for both. For values of $t \ll T_{\text{eff}}$ the exponential factor can be assumed to be unity.

The absorbed dose D_∞ for complete disintegration of a uniformly distributed γ -emitter is given by

$$D_\infty = K_\gamma \times \alpha_0 \times \frac{T_{\text{eff}}}{T_{1/2}} \times \rho \times g \quad [\text{rd}]$$

$$K_\gamma = 0.0338 \times T \times T_{1/2} \quad [\text{rd cm}^2 \mu\text{Ci}^{-1}]$$

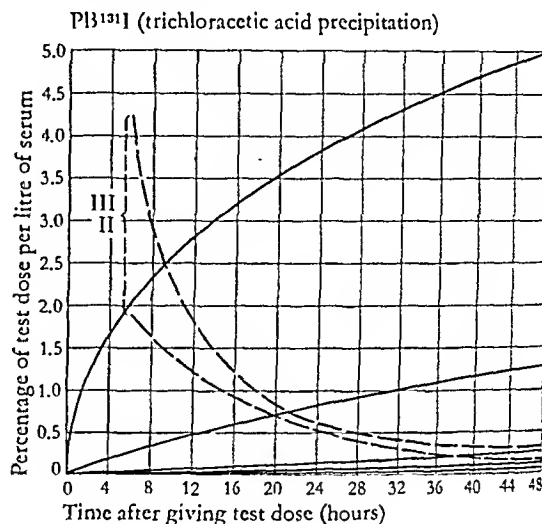
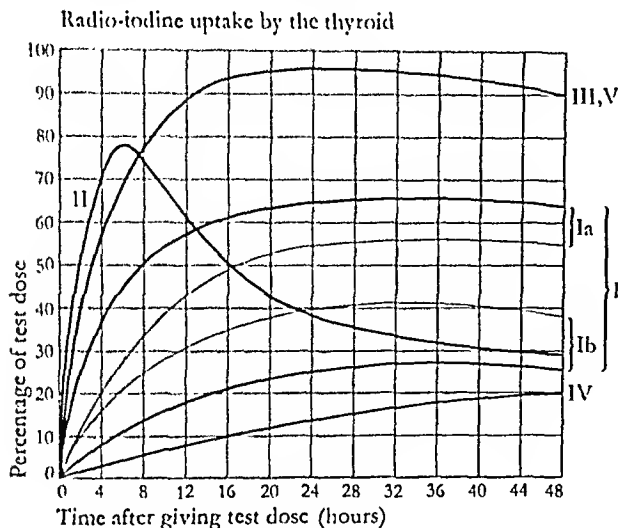
Typical radio-iodine test results

I Normal values

Ia Normal range in iodine-deficiency areas

Ib Normal range in iodine-surplus areas

- II Rapid iodine turnover in the rebound effect, severe hyperthyroidism, hereditary myxoedema (curves occasionally seen are shown by lines)
- III Hyperthyroidism (curves occasionally seen are shown by broken lines)
- IV Ingestion of drugs containing iodine, thyroid block, hypothyroidism
- V Iodine deficiency



where F is the fraction of $^{131}\text{I}-\text{T}_3$ taken up by the cells and H the haematocrit value.

In order to be able to compare T_{11} values with older values in the literature converted to a normal haematocrit value of 40% (T_{40}), WECHSELBERGER *et al.*⁶ have introduced another coefficient K' : $T_{40} = T_{11} + K'$. K' is calculated from one of the following two formulae, depending on whether the pathological haematocrit is above or below 40%:

For $H = 20-40\%$, $K' = +0.15 (40 - H)$

For $H = 40-80\%$, $K' = -6.5 \times 10^{-3} (H^2 - 50H + 400)$

K' values for various values of H are as follows:

H	K'	H	K'	H	K'
20%	+3.00	45%	-1.13	70%	-11.70
25%	+2.25	50%	-2.60	75%	-14.78
30%	+1.50	55%	-4.38	80%	-18.20
35%	+0.75	60%	-6.50		
40%	+0.00	65%	-8.93		

Variants of the T_3 test often use synthetic resins, dextran gels and other adsorbents in place of erythrocytes. Whatever form the test takes, however, the adsorption of free T_3 depends mainly on two variables: the concentration of T_4 or any other substance capable of displacing T_3 , and the TBG, prealbumin and albumin concentrations. The concentration of T_3 in the plasma usually has practically no effect. When the various extrathyroidal factors affecting the results are allowed for, relative T_{11} values of over 16-17% point in all probability to hyperthyroidism, values below 10-12% to hypothyroidism. Normal values fluctuate slightly, depending on how often the erythrocytes are washed and other procedural differences.

During pregnancy the T_{11} value is greatly decreased, often also during menstruation. Pathological values are seen in some extrathyroidal diseases, particularly disturbances of the plasma proteins, some types of leukaemia, and uraemic, hepatic and diabetic coma. The following drugs also affect the T_{11} value: anabolic agents, androgens, anticoagulants, corticosteroids, diphenylhydantoin, Evans blue, furosemide, gestagens (ovulation inhibitors), oestrogens, phenothiazine, phenylbutazone and derivatives, salicylates, sulphobromophthalcin, sulphonamides, thyroxine, tri-iodothyronine and thyrotropin, as well as many radionuclides given for diagnostic or therapeutic purposes.

'Free' thyroxine in blood⁷

The serum of euthyroidal persons contains about 50 ng of tein-bound iodine per millilitre, made up principally of thyroxine (T_4). After addition of $^{131}\text{I}-\text{T}_4$, only about 0.05% of the activity is dialysable against aqueous buffer solution, the remainder 99.95% being fairly firmly bound to protein. It follows that the serum contains about 0.025 ng of dialysable ('free') T_4 per millilitre. In hyperthyroidism this is increased to about 0.13 ng/ml, in hypothyroidism decreased to about 0.004 ng/ml. Unlike the T_{11} the serum T_4 level changes little in pregnancy. Its determination is subject to the errors common to all chemical methods of determining protein-bound iodine.

Thyroxine metabolism⁸

In healthy subjects the biological half-life of intravenously injected $^{131}\text{I}-\text{T}_4$ after reaching diffusion equilibrium is about 7 days. The extrathyroidal reserve of T_4 has been estimated at 80% of which about 100 μg is broken down per day. In hyperthyroidism the extrathyroidal T_4 reserve is increased to about 1800 μg in the augmented rate of breakdown (about 330 $\mu\text{g}/\text{day}$; half about 4 days). In hypothyroidism the reserve is reduced to about 360 μg , and the rate of breakdown to about 30 $\mu\text{g}/\text{day}$, with half-life increased to about 8½ days. Determination of the rapid rate of disappearance of $^{131}\text{I}-\text{T}_4$ is also of value in differential diagnosis. In vivo studies of T_4 are subject to interference by disturbances of liver function and by changes in the protein binding.

Thyroid scintigraphy

Two methods of obtaining scintigrams of the thyroid are in current use. In the older and more usual method a collimated scintillation crystal scans the thyroid in a horizontal plane. The impulses picked up are recorded simultaneously on paper, in some instruments in different colours showing the rate at which the impulses are received. The other method (scintillation camera) uses either a very large, fixed scintillation crystal about 25 cm in diameter carrying some 20 photomultipliers, or a group of ten or more scintillation detectors which scan the object simultaneously. The pulses are usually stored for a period ranging from a few seconds to minutes before being converted into a photographic image.

The principal radioactive sources used in thyroid scintigraphy are $^{131}\text{I}-$ and $^{99}\text{Tc}^{101}\text{O}_4^-$. ^{131}I scintigraphy is usually combined with the radio-iodine test, the scintigram being taken 12-48 hours after giving a test dose of 30 μCi Na^{131}I (2-10 μCi in children).

Although the use of ^{99}Tc requires a tenfold larger dose, the magnitude of the radiation load on the thyroid is about 100 times

ated by enteral loss of protein the over 10%. Although ^{51}Cr -human polymer it is the indicator of choice tant and medium half-life.

1213

d the gastrogenic 'intrinsic factor', s absorbed from the diet and from im, whence it is transported to the 84). Since the liver can store addi- *g's test uses an oral dose of 0.1-0.5* (1-0.5 μCi) given to the fasting pa- sular injection of 1000 μg cyano- saturate the liver and serum pro- t, the kidneys now excrete over 5% dministered. If the renal excretion eated a week later with the simul- s factor. If the renal excretion is re is a deficiency of intrinsic factor, y of the gastric mucosa and carci- ll low the patient is suffering from

serve amounts to about 40 mg/kg 0 mg/kg body weight, so that the 4 g of iron. The dose of 5-10 μCi metabolic iron studies is therefore ke of iron is about 17 mg, of which d. The daily iron turnover in the f 7-15 g of transferrin and 2-5 mg ies more than the amount absorbed anover can be calculated from the nd the biological half-life (T_b) of r 100 ml of whole blood in accor- la

transferrin binding, ^{51}Fe passes into 120 minutes, and within 8-24 hours he bone marrow. Within 6-14 days itered has reappeared in the blood

Extramedullary blood-forming ealed by radioactivity measure- spleen. Determination of the ferro- bservation time of 2-4 weeks

rate of disappearance of tagged 0-95% of the chromium of which f globin, the amount depending on s takes 10-25 days and requires a normal adults the half-life of the 24-35 days). At the same time the r and serum is determined by sur- ie uptake by the spleen must be leen/liver activity ratio exceeds 1.2 measured at the same time as the metely 1-3 activity measurements s 10-20 minutes after intravenous

^{51}Cr -tagged erythrocytes For nor,

rapidly and simply determined by) μCi of tagged (^{101}I , ^{125}I) human or of 10-30 μCi of ^{51}Cr -albumin after the injection the rate at which plasma is mainly dependent on the ean with the normal protein in the is a gradual movement of activity y extrapolating the activity curve n the activity concentration at the approximately calculated For nor.

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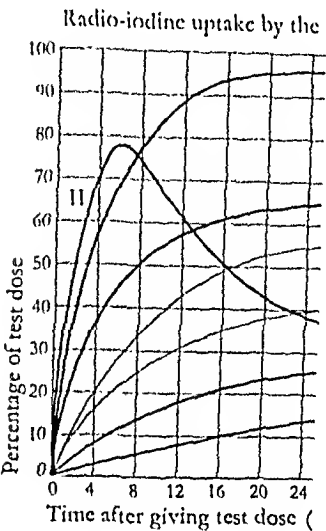
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Typical radio-iodine test results

- I Normal values
- Ia Normal range in iodine-deficiency
- Ib Normal range in iodine-surplus



where F is the fraction of $^{131}\text{I}-\text{T}_3$ haematocrit value.

In order to be able to compare literature converted to a normal WECHSELBERGER et al.⁶ have introduced $T_{40} = T_{31} + K'$. K' is calculated from formulae, depending on whether the value is above or below 40%:

- For $H = 20-40\%$, $K' = + 0.15$
- For $H = 40-80\%$, $K' = - 6.5$

brings
inflammation
under control



ins, particularly the 'toxic' variety, have a largely autonomous metabolism independent of anterior pituitary control, suppression three days with daily doses of 50-100 µg of tri-iodothyronine

led inflammatory areas in a goitrous gland.
or whole-body scintigraphy aimed at locating an aberrant goitre

y when there is no danger of compression.

kidneys

Radiography of the kidneys at present makes use principally of diethylenetriaminepentaacetic acid (DTPA). With ^{111}In DTPA the applied dose is about 1 µCi/kg body weight, with ^{113}In DTPA usually 0.4 µCi/kg body weight. The nephrogram reveals two main phases, both of which can be evaluated.

(a) A rising phase commencing about 10-15 seconds after the injection and reaching a maximum in 4-6 minutes. This phase represents the uptake, storage and secretion of the DTPA and can often be divided into a very steep part (initial phase) and rather less steep part (functional phase) separated by a more or less sharp break.

(b) A falling phase commencing about 10-15 minutes after the injection and reaching a minimum in 4-6 hours. This phase represents the excretion of the DTPA and can often be divided into a very steep part (initial phase) and rather less steep part (functional phase) separated by a more or less sharp break.

Details are shown up better with ^{201}Tl or ^{113}In -chloromerodiphenylacetic acid than with ^{111}In DTPA.

liver

Intravenous injection of 10-30 µCi ^{111}In Bengal red is followed

minutes the activity is concentrated in the gallbladder region. The rise and fall in the activity are determined by the blood flow and functional capacity of the liver. Scintigraphy of the liver can also be carried out with colloidal radiogold (^{198}Au , 40-100 µCi i.v.), which is phagocytosed by the cells of the reticuloendothelial system but this isotope gives no picture of the gallbladder.

brain

Scintigraphy of the brain is performed by the injection of a small amount of a tracer into the cerebrospinal fluid. The tracer is then taken up by the brain tissue and the activity is concentrated in the brain. The rise and fall in the activity are determined by the blood flow and functional capacity of the brain. Scintigraphy of the brain can also be carried out with colloidal radiogold (^{198}Au , 40-100 µCi i.v.), which is phagocytosed by the cells of the reticuloendothelial system but this isotope gives no picture of the gallbladder.

Gastroenterology

Excretion of plasma proteins or polyvinylpyrrolidone (PVP) ^{125}I

In 4 days, normal persons excrete 0.3-1.0% of a tracer dose of 5-10 µCi ^{125}I -PVP or 20-30 µCi ^{125}I -albumin in the faeces. After 6 days the upper limit of the total activity excreted is about 1.5%.

Radioimmunological methods¹⁷

Insulin antibodies

Humoral antibodies in the γ -globulin range that reversibly adsorb insulin instead of precipitating it appear in the blood of only those persons who have previously been given this drug - usually during the 3-6 weeks after the first insulin injection. The binding capacity of these antibodies can be determined by electrophoretic, chromatographic or adsorption-equilibrium methods using insulin tagged with radio-iodine. Binding capacities of over 0.8-1.0 mg of ^{131}I -insulin per litre serum (≈ 20 -25 IU/l serum) are often, but not always, associated with intractable diabetes, very high values with insulin resistance. These antibodies are active not only against the homologous (sensitizing) insulin but also against insulin from other species. Thus anti-beef insulin human γ -globulin - formed in man when beef insulin is injected - binds not only the latter but also human and hog insulins. All quantitative immunological methods of determining the concentration of the hormone depend both on this nonspecificity and on the reversibility of the antigen-antibody binding.

Determination of hormone levels

Nonprecipitating antibodies to insulin and other hormone antigens are usually obtained from guinea-pigs. These antibodies bind the corresponding tagged hormones reversibly, for addition of non-radioactive hormone antigen causes the tagged hormone to be displaced from its binding with the species-nonspecific antibody. The higher the concentration of hormone, the less therefore is the amount of antigen activity carried by the antibody γ -globulins. The γ -globulin-hormone complexes can be separated from the unbound ('free') hormone by electrophoresis, chromatography, the adsorption-equilibrium method, immunoprecipitation or other selective precipitation techniques. Hormones that are adequately homogeneous and particularly suitable for determination by radio-immunological methods are insulin, glucagon, ACTH and growth hormone. The lower limit of determination lies in the nanogramme to picogramme range and is dependent on the specific activity of the tagged hormone antigens (5-50 mCi of radio-iodine per milligramme of hormone) and on the hormone-binding capacity of the antibody γ -globulins.

Therapeutic uses¹

In contrast to the natural radioactive isotopes, which on account of their gaseous decay products can only be used for therapeutic purposes when enclosed in a gastight container (needles, tubes or plaques of platinum, gold or monel metal), the artificial isotopes can mostly be used without enclosure and in either the solid or liquid form. The placing of the radioisotope in a circumscribed focus of disease with maximum possible protection of the surrounding healthy tissue can be achieved by various methods.

Teletherapy (γ -emitters)

Isotope ^{60}Co . Sources with a specific activity of 20-100 Ci/g are used, usually as cylinders 10 \times 10 mm up to 25 \times 25 mm. The source as purchased is fully shielded in a tungsten or lead container, the emergent radiation being controlled by an adjustable or exchangeable tungsten diaphragm. Exposure time is adjusted by a remote-

therapy. Crossfire technique, rotation therapy or arc therapy. Advantages over 200 kV X-ray therapy are: higher relative depth dose; sharper lateral limitation of the field; absorption in bone practically the same as in soft tissues (less injury to the bones); maximum dose 4-5 mm beneath the skin (dose on skin surface 25-30% of maximum, with correspondingly milder skin reaction). The biological effectiveness of the radiation from ^{60}Co is about 80% of that of 200 kV X rays, so that the dosages given are usually somewhat higher.

Isotope ^{137}Cs . Sources may be contaminated with the shorter-lived isotope ^{134}Cs (half-life 2.3 y compared with 30 y for ^{137}Cs), in which case there is a more rapid loss of activity. The advantage of this isotope lies in its longer half-life than ^{60}Co ; its disadvantages are its much lower specific activity, necessitating larger sources and therefore larger penumbra, and its lower γ -energy, resulting in more injury to the skin and bones.

Contact therapy (β - and γ -emitters)

Pure β -emitters are used for the irradiation of surface foci in dermatology and ophthalmology and are applied directly to the lesion in suitable forms.

Isotope ^{32}P and $^{90}\text{Sr}/^{90}\text{Y}$. Maximum depth of penetration 5 effective range ca. 3 mm. Commercially available in the form of flexible plastic foils containing 20% red phosphorus which become activated in a reactor.

The Sr/Y mixture is available in metal capsules with a silver filter over the exit surface. Activity is due to the β -radiation daughter isotope ^{90}Y . Ophthalmological applicators shape the corneal curvature are available.

A greater depth effect is obtained with γ -emitters applied to the surface to be treated. Commercially available is ^{60}Co granules of soft plastic mass (Plastobalt) or as plastic spheres enclosed in gold foil. These provide optimal adaptation to surfaces of any shape. The dose of γ -emitters decreases sharply with increasing depth since the intensity is inversely proportional to the square of the distance. ^{182}Tl is available in the form of wire in a plastic and is particularly suitable for ring sources for epibulbar irradiation.

Interstitial irradiation

Needles of solid γ -emitters. ^{60}Co is supplied as wire of the alloy 'Cobanic' (55% nickel + 45% cobalt) in steel needles or tubes. These 'threads' are sewn into the lesion and have many advantages over rigid carriers.

^{182}Tl wire (0.4 mm diameter with platinum envelope 0.1 mm thick) is formed into hairpin-shaped loops which are inserted into tumour tissue, particularly in the wall of the bladder.

^{192}Ir is also very suitable for interstitial application in this form. The threads are withdrawn from the tissues at the end of the irradiation period.

For tumours accessible for only a short time, 'seeds' of radioisotope (^{198}Au) ca. 2.5 mm long and 0.8 mm in diameter are used, the radiation being filtered out by means of an inactive gold or platinum coating. Such seeds can be quickly and accurately placed in tissue with the aid of a 'pistol' for which filled 'magazines' are available. The magazines must be sterilized before placing in the pistol. Another equipment allows pieces of any desired length to be cut under shielding from radiogold wire coated with inactive gold. The pieces are then inserted into the tissue through a special catheter. Radiogold seeds have important advantages over radon seeds.

Needles of solid β -emitters. ^{90}Y (pure β -emitter) in the form of ceramic bodies (1 mm Y_2O_3 spheres) is particularly suitable for the irradiation of the pituitary, either via the nose or by stereotactic techniques. Uniform distribution of the dose over the pituitary can be achieved by implanting about 40 spheres. The total dose required for radiohypophysectomy is about 10 mCi.

Infiltration methods (β -emitters). The radioactive substance is injected directly into the tumour tissue in the form of a stable colloidal solution. The irradiation can be assumed to be practically homogeneous when the individual deposits are not more than 3 mm apart. Isotopes used: colloidal radiogold (^{198}Au), colloidal ^{32}P , $^{32}\text{CrPO}_4$, colloidal ^{90}Y . There is some loss of activity via the lymphatics with concentration in the neighbouring lymph glands.

For dosage calculation see pages 286 and 287.

Intracavitary irradiation

(a) Colloidal suspensions of radiogold (^{198}Au) are used for intraperitoneal and intrapleural infusion in superficial or disseminated carcinomatosis. Individual doses of 100-150 mCi are given, repeated if necessary after several months up to a total dose of 500 mCi. The main activity is due to the β -radiation, with a small depth effect up to ca. 3 mm. This technique has recently been used for irradiation of the inner wall of the bladder, using 300 mCi of radiogold for 4-hour period. The dosage can be obtained from a nomogram.

(b) Solid applicators in the form of plastic masses containing ^{60}Co grains of diameter ca. 1 mm are used principally for irradiation of tumours of the mouth, nose and pharyngeal cavities. Beads of ^{60}Co of diameter 6 mm are strung together for insertion into the oesophagus, or can be packed into natural or surgically opened body cavities.

(c) Gynaecology: Scaled radium carriers (platinum filter capsules) of total content 50-130 mg of ^{226}Ra introduced into the vagina, cervix and/or uterus.

Enteral and intravenous applications

A therapeutic effect from intravenous or peroral administration of isotopes is only obtainable when the isotope can be concentrated

Characteristics of radioactive nuclides with medical applications¹

Nuclide	Half-life	Mode of decay	β -Radiation		E_{β}^{tot}	γ -Radiation ² (energies in MeV)	Dose constants					β -range in water ³ (mm)	Reciprocal specific activity ⁴ $\left[\frac{\text{PS}}{\mu\text{Ci}}\right]$
			E_{max}	\bar{E}_{β}			K_{β} $\left[\frac{\text{rd g}}{\mu\text{Ci}}\right]$	Γ $\left[\frac{\text{R cm}^2}{\text{h } \mu\text{Ci}}\right]$	K_{γ} ³ $\left[\frac{\text{rd cm}^2}{\mu\text{Ci}}\right]$				
¹ H	12.36 y	β^-	0.018 (100)	0.005 _s	0.005 _s	-	1835	-	-	10	11	103	
¹⁴ C	5568 y	β^-	0.156 (100)	0.049 _s	0.049 _s	-	7450 $\times 10^3$	-	-	-	0.007	218 $\times 10^3$	
²² Na	2.58 y	β^+ , EC, γ	+0.54 (89)	0.188	0.188	1.28 (100); 0.51 (178)	13100	11.7	3.72 $\times 10^2$	-	0.24	160	
²⁴ Na	15 h	β^- , γ	1.39 (100)	0.550	0.550	2.75 (100); 1.37 (100)	25.6	18.1	0.39	-	2.1	0.113	
³² P	14.4 d	β^-	1.71 (100)	0.695	0.695	-	739	-	-	-	6.4	3.52	
³⁵ S	87.5 d	β^-	0.167 (100)	0.049	0.049	-	316	-	-	-	8.0	23.4	
³⁶ Cl	2.85 $\times 10^5$ y	β^- , EC	0.71 (98)	0.247	0.247	-	1900 $\times 10^3$	-	-	-	0.3	30.5 $\times 10^3$	
⁴² K	12.47 h	β^- , γ	3.55 (82); 1.98 (18)	1.469	1.469	1.53 (18)	56.3	1.35	0.024	-	2.7	0.167	
⁴⁵ Ca	159 d	β^-	0.258 (100)	0.078	0.078	-	915	-	-	-	19	0.6	
⁴⁷ Ca	4.7 d	β^- , γ	2.00 (18); 0.69 (82)	-	-	1.30 (76); 0.81 (6); 0.50 (6)	-	-	-	-	0.6	56.6	
⁵¹ Cr	27.8 d	EC, γ	-	-	0.0049	0.32 (9)	10	5.1	0.81	-	9.6	1.69	
⁵² Mn	5.67 d	β^+ , EC, γ	+0.58 (34)	0.084 _s	0.088	1.46 (100); 0.94 (100); 0.73 (100); 0.51 (68)	36.9	0.18	0.17	-	-	10.9	
⁵⁴ Mn	297 d	EC, γ	-	-	0.0054	0.84 (100)	118.7	18.5	3.6	-	2.2	2.27	
⁵⁵ Fe	2.77 y	EC	-	-	0.0059	-	441	4.7	47	-	-	122.6	
⁵⁷ Co	267 d	EC, γ	-	-	-	0.136 (9); 0.122 (89); 0.0144 (6)	-	-	-	-	-	414	
⁵⁸ Co	71 d	β^+ , EC, γ	+0.49 (15)	-	-	1.6 (5); 0.81 (99.5); 0.51	-	0.61	5.5	-	-	118	
⁵⁹ Fe	45 d	β^- , γ	1.56 (0.3); 0.462 (54); 0.271 (46)	0.128	0.128	1.29 (43); 1.10 (57); 0.19 (3)	432	5.585	13.4	-	1.5	31.6	
⁶⁰ Co	5.23 y	β^- , γ	1.48 (0.2); 0.312 (99.8)	0.095	0.095	1.33 (100); 1.17 (100)	1340	6.2	9.4	-	1.5	20.6	
⁶⁴ Cu	12.8 h	β^- , β^+ , EC, γ	0.57 (39); +0.65 (19)	0.126	0.130	1.35 (0.5); 0.51 (38)	5.1	12.9	8.32 $\times 10^2$	-	0.8	884	
⁶⁵ Zn	245 d	β^+ , EC, γ	+0.324 (1.5)	0.002	0.010	1.12 (46); 0.51 (3)	181	1.15	0.021	-	2.6	0.226	
⁷¹ As	18 d	β^- , β^+ , EC, γ	1.36 (17.7); 0.72 (14.5); +1.5 (3.6); +0.91 (26.1)	-	-	0.635 (14.5); 0.596 (61); 0.51	-	2.8	23	-	1.2	122	
⁷⁵ Se	120 d	EC, γ	-	-	-	0.405 (15); 0.308 (1); 0.281 (28); 0.269 (54); 0.20 (2); 0.136 (40); 0.122 (12); 0.097 (2); 0.066 (7) and other weak lines	-	4.4	2.6	-	7.0	9.93	
⁷⁶ Se	26.45 h	β^- , γ	2.97 (50); 2.41 (31); 1.76 (16); 0.36 (3)	1.078	1.078	2.06 (2); 1.41 (1); 1.21 (12); 0.65 (5); 0.56 (38)	87.8	1.5	6.1	-	-	69	
⁸¹ Br	35.7 h	β^- , γ	0.45 (100)	0.134	0.134	1.48 (17); 1.32 (28); 1.04 (27); 0.83 (27); 0.78 (83); 0.70 (27); 0.62 (44); 0.55 (73)	14.7	2.4	0.089	-	15.7	0.642	
⁸¹ Kr	10.6 y	β^- , γ	0.672 (<99.3); 0.15 (>0.7)	0.627	0.627	0.514 (~0.7)	-	14.5	0.73	-	1.6	0.942	
⁸⁶ Rb	18.66 d	β^- , γ	1.78 (84); 0.71 (15); 0.23 (1)	0.555	0.555	1.08 (9)	864	0.02	2.6	-	2.5	2520	
⁹⁰ Sr	51.5 d	β^-	1.46 (100)	0.174	0.174	-	2260	0.51	0.32	-	8.7	12.3	
⁹⁰ Sr	28.0 y	β^-	0.54 (100)	0.917	0.917	-	(1510 $\times 10^3$)	-	-	-	6.8	34.7	
⁹⁰ Y	64.5 h	β^-	2.26 (100)	0.917	0.917	-	182	-	-	-	2.2	7050	
⁹⁹ Tc	67 h	β^- , γ	1.23 (85); 0.87 (~1); 0.45 (14)	0.917	0.917	0.780 (4); 0.741 (10); 0.181 (2); 0.041 (1)	-	-	-	-	11	1.86	

Nuclide	Half-life	Mode of decay	β-Radiation		E_{β}^{tot}	γ-Radiation ² (energies in MeV)	Dose constants			β-range in water ³ (mm)	Reciprocal specific activity ⁴ $\left[\frac{\mu\text{Ci}}{\text{g}}\right]$	
			E_{\max}	\bar{E}_{β}			K_{β} $\left[\frac{\text{rd g}}{\mu\text{Ci}}\right]$	Γ $\left[\frac{\text{R cm}^2}{\text{h } \mu\text{Ci}}\right]$	K_{γ}^3 $\left[\frac{\text{rd cm}^2}{\mu\text{Ci}}\right]$			
³ H	12.36 y	β ⁻	0.018 (100)	0.005 _s	0.005 _s	-	1835	-	-	11	0.007	103
¹⁴ C	5568 y	β ⁻	0.156 (100)	0.049 _s	0.049 _s	-	7450 × 10 ³	-	-	11	0.24	218 × 10 ³
²² Na	2.58 y	β ⁺ , EC, γ	+0.54 (89)	0.188	0.188	1.28 (100); 0.51 (178)	13100	11.7	3.72 × 10 ²	10	2.1	160
²⁴ Na	15 h	β ⁻ , γ	1.39 (100)	0.550	0.550	2.75 (100); 1.37 (100)	25.6	18.1	0.39	10	6.4	0.113
³² P	14.4 d	β ⁻	1.71 (100)	0.695	0.695	-	739	-	-	10	8.0	3.52
³⁵ S	87.5 d	β ⁻	0.167 (100)	0.049	0.049	-	316	-	-	10	0.3	23.4
³⁶ Cl	2.85 × 10 ⁵ y	β ⁻ , EC	0.71 (98)	0.247	0.247	-	1900 × 10 ³	-	-	10	2.7	30.5 × 10 ³
⁴² K	12.47 h	β ⁻ , γ	3.55 (82); 1.98 (18)	1.469	1.469	1.53 (18)	56.3	1.35	0.024	10	19	0.167
⁴⁵ Ca	159 d	β ⁻	0.258 (100)	0.078	0.078	-	915	-	-	10	0.6	56.6
⁴⁷ Ca	4.7 d	β ⁻ , γ	2.00 (18); 0.69 (82)	-	-	1.30 (76); 0.81 (6); 0.50 (6)	-	5.1	0.81	10	9.6	1.69
⁵¹ Cr	27.8 d	EC, γ	-	-	0.0049	0.32 (9)	10	0.18	0.17	10	-	10.9
⁵² Mn	5.67 d	β ⁺ , EC, γ	+0.58 (34)	0.084 _s	0.088	1.46 (100); 0.94 (100); 0.73 (100); 0.51 (68)	36.9	18.5	3.6	10	2.2	2.27
⁵⁴ Mn	297 d	EC, γ	-	-	0.0054	0.84 (100)	118.7	4.7	47	10	-	122.6
⁵⁵ Fe	2.77 y	EC	-	-	0.0059	-	441	-	-	10	-	414
⁵⁷ Co	267 d	EC, γ	-	-	-	0.136 (9); 0.122 (89); 0.0144 (6)	-	0.61	5.5	10	-	118
⁵⁸ Co	71 d	β ⁺ , EC, γ	+0.49 (15)	-	-	1.6 (5); 0.81 (99.5); 0.51	-	5.585	13.4	10	1.5	31.6
⁵⁹ Fe	45 d	β ⁻ , γ	1.56 (0.3); 0.462 (54); 0.271 (46)	0.128	0.128	1.29 (43); 1.10 (57); 0.19 (3)	432	6.2	9.4	10	1.5	20.6
⁶⁰ Co	5.23 y	β ⁻ , γ	1.48 (0.2); 0.312 (99.8)	0.095	0.095	1.33 (100); 1.17 (100)	1340	12.9	8.32 × 10 ²	10	0.8	884
⁶⁴ Cu	12.8 h	β ⁻ , β ⁺ , EC, γ	0.57 (39); +0.65 (19)	0.126	0.130	1.35 (0.5); 0.51 (38)	5.1	1.15	0.021	10	2.6	0.226
⁶⁵ Zn	245 d	β ⁺ , EC, γ	+0.324 (1.5)	0.002	0.010	1.12 (46); 0.51 (3)	181	2.8	23	10	1.2	122
⁷⁴ As	18 d	β ⁻ , β ⁺ , EC, γ	1.36 (17.7); 0.72 (14.5); +1.5 (3.6); +0.91 (26.1)	-	-	0.635 (14.5); 0.596 (61); 0.51	-	4.4	2.6	10	7.0	9.93
⁷⁵ Se	120 d	EC, γ	-	-	-	0.405 (15); 0.308 (1); 0.281 (28); 0.269 (54); 0.20 (2); 0.136 (40); 0.122 (12); 0.097 (2); 0.066 (7) and other weak lines	-	1.5	6.1	10	-	69
⁷⁶ As	26.45 h	β ⁻ , γ	2.97 (50); 2.41 (31); 1.76 (16); 0.36 (3)	1.078	1.078	2.06 (2); 1.41 (1); 1.21 (12); 0.65 (5); 0.56 (38)	87.8	2.4	0.089	10	15.7	0.642
⁸² Br	35.7 h	β ⁻ , γ	0.45 (100)	0.134	0.134	1.48 (17); 1.32 (28); 1.04 (27); 0.83 (27); 0.78 (83); 0.70 (27); 0.62 (44); 0.55 (73)	14.7	14.5	0.73	10	1.6	0.942
⁸³ Kr	10.6 y	β ⁻ , γ	0.672 (< 99.3); 0.15 (> 0.7)	0.627	0.627	0.514 (~0.7)	864	0.02	2.6	10	2.5	2520
⁸⁶ Rb	18.66 d	β ⁻ , γ	1.78 (84); 0.71 (15); 0.23 (1)	0.555	0.555	1.08 (9)	2260	0.51	0.32	10	8.7	12.3
⁸⁹ Sr	51.5 d	β ⁻	1.46 (100)	0.174	0.174	-	-	-	-	10	6.8	34.7
⁹⁰ Sr	28.0 y	β ⁻	0.54 (100)	0.174	0.174 (0.20)	-	-	-	-	10	2.2	7050
⁹⁰ Y	64.5 h	β ⁻	2.26 (100)	0.917	0.917	-	182	-	-	10	11	1.86
⁹³ Nb	67 h	β ⁻ , γ	1.23 (85); 0.87 (~1); 0.45 (14)	0.917	0.917	0.780 (4); 0.741 (10); 0.181 (2); 0.041 (1)	-	0.73	0.17	10	5.4	2.16

¹³⁷ Cs	6 h	γ	-	0.142 (1), 0.140 (88)	0.67	0.0037	-	0.19
^{137m} Ag	7.5 d	β ⁺ , γ	0.356	0.34 (8), 0.24 (1)	197	0.043	4.0	6.35
^{137m} Sn	119 d	EC, γ	0.120	0.39 (69)	1058	13	11.7	103
^{137m} Te	17 d	EC, γ	-	0.009	6.3	2.5	-	15.7
^{137m} Sb	60.5 d	β ⁺ , γ	0.371	0.371	1666	19	4.1	57
^{137m} I	60 d	EC, γ	-	0.035 (7) [0.027 (93) Te X rays]	0.67	1.35	-	57
^{137m} I	12.5 h	β ⁺ , γ	0.267	1.15 (31), 0.74 (69), 0.66 (100); 0.53 (100), 0.41 (23)	12.1	0.21	4.5	0.52
^{137m} I	8.09 d	β ⁺ , γ	0.188	0.722 (3), 0.637 (9), 0.364 (80), 0.294 (5), 0.08 (2)	2.2	0.60	2.2	8.1
^{137m} I	2.3 h	β ⁺ , γ	-	1.40 (8), 1.14 (4), 0.95 (19), 0.78 (82), 0.72 (7), 0.67 (99), 0.65 (26), 0.62 (5); 0.52 (19) and other weak lines	11.12	0.036	10.7	0.095
^{137m} Te	78 h	β ⁺ , γ	0.22 (100)	0.23 (92), 0.052 (-16)	12.74	1.4	0.5	3.23
^{137m} Cs	30 y	β ⁺ , γ	0.179	0.662 (84)	1900 × 10 ⁴	1.2 × 10 ⁴	9.0	10.900
^{137m} Tm	120 d	β ⁺ , EC, γ	0.323	0.084 (9)	2860	0.3	4.0	156
^{137m} Ta	113 d	β ⁺ , γ	0.142	1.23, 1.22, 1.19, 1.12, 0.22, 0.15, 0.10, 0.07 and other weak lines	1183*	6.0	1.8	159
^{137m} Ir	74.5 d	β ⁺ , EC	0.169	0.61, 0.60, 0.48, 0.47, 0.32, 0.31, 0.30, and other weak lines	930*	5.0	2.5	109
^{137m} Hg	65.5 h	EC, γ	-	1.92 (1), 0.077 (28)	2.4	0.06	-	4.08
^{137m} Au	2.7 d	β ⁺ , γ	0.312	1.09 (0.3), 0.67 (1.2), 0.41 (97)	64.0	0.21	3.8	4.1
^{137m} As	3.15 d	β ⁺ , γ	0.085	0.208 (16), 0.158 (77), 0.05 (0.6)	26.4	0.09	1.5	4.8
^{137m} Hg	46.5 d	β ⁺ , γ	0.057	0.279 (66)	296	2.15	0.45	73.3
^{137m} Tl	4.1 y	β ⁺ , EC	0.238	-	263 × 10 ⁴	0.007	2.9	2330

• 3 Rays only

References

- Modified from GLUCKER and MACHFRAUCH, *Reagenz und Kryptanalyse für Mathematiker und Physiker*, 2nd ed., Thieme, Stuttgart, 1965, pages 39, 40, 42 and 238.

Notes

- Column 3* β^+ — positron emission, EC — orbital electron capture
- Column 4* E_{\max} — maximum β -energy in MeV \rightarrow positron emission. Numbers in brackets are the frequencies of electron or positron emission as percentage of disintegrations
- Column 5* E_K — mean value of the energies of all the β -rays emitted per disintegration. Calculated from the data of theoretical data of I. H. Maxmuth (Nudolov, 12, 34 (1953))
- Column 6* $E_{\text{int}}^{\text{sum}}$ — sum of E_K , the K energy (from internal conversions and electron capture), the energies of the conversion and Auger electrons, and the L and M energies. For nuclides with atomic numbers greater than 82, the K energy is usually insufficient in calculating the γ dose. For ^{137}Cs and ^{137}Ba a correction factor of 1.17 to take account of forbidden transitions.

Explanation of the tables on pages 294-306 *

Column 1 t - elapsed time ($t - t_0$) in days (d), hours (h) and minutes (min).

Column 2 N_t - amount of isotope not disintegrated at time t expressed as percentage of N_0 (the values apply equally to the activities A_t and A_0).

Columns 3 and 4 Factors and their logarithms for calculating N_0 (or A_0) from N_t (or A_t):

$$N_0 = \frac{N_t}{f} \quad \text{or} \quad A_0 = \frac{A_t}{f}$$

The half-lives ($T_{1/2}$) of $^{99}\text{Tc}^m$, ^{132}Te and ^{192}Ir are taken from the *Handbook of Chemistry and Physics*¹, all others from the *Catalogue of Radioactive Products*².

* Reproduction of data on pages 294-306 only by permission of the publishers of these *Scientific Tables*.

Decay data for ^{211}H and ^{226}Ra have also been calculated and may be obtained on application to the publishers of these *Scientific Tables*.

The data in the tables have been calculated by computer using the following relationships (see also page 217):

$$\ln \frac{N_t}{N_0} = -\frac{\ln 2}{T_{1/2}} t$$

$$\ln \frac{N_0}{N_t} = \frac{\ln 2}{T_{1/2}} t$$

$$\left(\text{Disintegration constant } \lambda_t = \frac{\ln 2}{T_{1/2}} \right)$$

References

¹ HEATH, R. L., in WEAST et al. (Eds.), *Handbook of Chemistry and Physics*, 49th ed., The Chemical Rubber Co., Cleveland, 1968, page B-4.

² Radiochemical Centre, *Catalogue of Radioactive Products*, RC.11, Amersham, Bucks., 1967/68.

t				t				t				t																			
d				d h min				d h min				d h min																			
N _t				N ₀ /N _t				log ₁₀ N ₀ /N _t				N _t				N ₀ /N _t				log ₁₀ N ₀ /N _t											
Sodium-22																Sodium-24															
half-life 2.6 y																half-life 15 h															
0	100.00	1.000	0.00000	3	0	87.06	1.148	0.06021	20	49.24	2.031	0.30772	22	11.94	8.378	0.92315	2	0	10.88	9.189	0.96329										
50	96.42	1.037	0.01585	10	86.39	1.157	0.06355	30	48.86	2.046	0.31106	23	11.40	8.774	0.94322	1	1	10.39	9.623	0.98335											
100	92.96	1.076	0.03170	20	85.72	1.166	0.06690	40	48.48	2.062	0.31441	0	10.88	9.189	0.96329	2	2	9.92	10.079	1.00343											
150	89.63	1.116	0.04755	30	85.07	1.175	0.07024	50	48.11	2.078	0.31775	1	10.39	9.623	0.98335	3	3	9.47	10.556	1.02350											
200	86.42	1.157	0.06340	40	84.41	1.184	0.07359	16	0	47.74	2.094	0.32110	2	9.92	10.079	1.00343	4	4	9.05	11.055	1.04357										
250	83.32	1.200	0.07925	50	83.77	1.193	0.07693	10	47.38	2.110	0.32444	3	9.47	10.556	1.02350	5	5	8.64	11.578	1.06364											
300	80.33	1.245	0.09510	4	0	83.12	1.203	0.08028	20	47.01	2.127	0.32779	4	9.05	11.055	1.04357	6	6	8.25	12.125	1.08371										
400	74.68	1.339	0.12680	10	82.49	1.212	0.08362	30	46.65	2.143	0.33113	5	8.64	11.578	1.06364	7	7	7.87	12.699	1.10378											
500	69.42	1.440	0.15850	20	81.85	1.221	0.08696	40	46.29	2.160	0.33448	6	8.25	12.125	1.08371	8	8	7.52	13.299	1.12385											
600	64.54	1.550	0.19020	30	81.23	1.231	0.09031	50	45.94	2.176	0.33782	7	7.87	12.699	1.10378	9	9	7.18	13.928	1.14391											
700	59.99	1.667	0.22190	40	80.60	1.240	0.09365	17	0	45.59	2.193	0.34117	8	7.52	13.299	1.12385	10	10	6.86	14.587	1.16398										
800	55.77	1.793	0.25360	50	79.98	1.250	0.09700	10	45.24	2.210	0.34451	9	7.18	13.928	1.14391	11	11	6.55	15.277	1.18405											
900	51.84	1.929	0.28530	5	0	79.37	1.259	0.10034	20	44.89	2.227	0.34786	12	6.25	16.000	1.20412	12	12	6.25	16.000	1.20412										
1000	48.19	2.075	0.31700	10	78.76	1.269	0.10368	30	44.54	2.244	0.35120	13	5.97	16.756	1.22419	13	13	5.97	16.756	1.22419											
1100	44.80	2.232	0.34870	20	78.16	1.279	0.10703	40	44.20	2.262	0.35455	14	5.70	17.549	1.24426	14	14	5.70	17.549	1.24426											
1200	41.65	2.401	0.38040	30	77.56	1.289	0.11038	50	43.86	2.279	0.35789	15	5.44	18.379	1.26433	15	15	5.44	18.379	1.26433											
1300	38.72	2.583	0.41210	40	76.96	1.299	0.11372	18	0	43.53	2.297	0.36124	16	5.20	19.248	1.28439	16	16	5.20	19.248	1.28439										
1400	35.99	2.778	0.44380	50	76.37	1.309	0.11707	10	43.19	2.315	0.36458	17	4.96	20.158	1.30446	17	17	4.96	20.158	1.30446											
1500	33.46	2.989	0.47550	6	0	75.79	1.319	0.12041	20	42.86	2.333	0.36793	18	4.74	21.112	1.32453	18	18	4.74	21.112	1.32453										
1600	31.10	3.215	0.50720	10	75.20	1.329	0.12376	30	42.53	2.351	0.37127	19	4.52	22.110	1.34460	19	19	4.52	22.110	1.34460											
1800	26.88	3.720	0.57060	20	74.63	1.339	0.12710	40	42.21	2.369	0.37462	20	4.32	23.156	1.36467	20	20	4.32	23.156	1.36467											
2000	23.23	4.305	0.63400	30	74.05	1.350	0.13045	50	41.88	2.387	0.37796	21	4.12	24.251	1.38474	21	21	4.12	24.251	1.38474											
2250	19.35	5.167	0.71325	40	73.49	1.360	0.13379	19	0	41.56	2.406	0.38131	22	3.94	25.398	1.40481	22	22	3.94	25.398	1.40481										
2500	16.13	6.201	0.79250	50	72.92	1.371	0.13714	10	41.24	2.424	0.38465	23	3.76	26.599	1.42488	23	23	3.76	26.599	1.42488											
2750	13.44	7.443	0.87175	7	0	72.36	1.381	0.14048	20	40.93	2.443	0.38799	3	3.59	27.857	1.44494	3	3	3.59	27.857	1.44494										
3000	11.19	8.933	0.95100	10	71.81	1.392	0.14383	30	40.61	2.462	0.39134	4	3.43	29.175	1.46501	4	4	3.43	29.175	1.46501											
3250	9.33	10.721	1.03025	20	71.26	1.403	0.14717	40	40.30	2.481	0.39468	5	3.27	30.554	1.48508	5	5	3.27	30.554	1.48508											
3500	7.77	12.868	1.10949	30	70.71	1.414	0.15052	50	39.99	2.500	0.39803	6	3.13	32.000	1.50515	6	6	3.13	32.000	1.50515											
3750	6.48	15.443	1.18874	40	70.17	1.425	0.15386	10	39.69	2.519	0.40137	7	2.98	33.513	1.52522	7	7	2.98	33.513	1.52522											
4000	5.40	18.535	1.26799	50	69.63	1.436	0.15720	20	39.38	2.539	0.40472	8	2.85	35.098	1.54529	8	8	2.85	35.098	1.54529											
4250	4.50	22.246	1.34724	8	0	69.10	1.447	0.16055	30	39.08	2.558	0.40806	9	2.72	36.758	1.56536	9	9	2.72	36.758	1.56536										
4500	3.75	26.699	1.42649	10	68.57	1.458	0.16389	40	38.78	2.578	0.41141	10	2.60	38.496	1.58543	10	10	2.60	38.496	1.58543											
4750	3.12	32.044	1.50574	20	68.04	1.469	0.16724	50	38.48	2.598	0.41475	11	2.48	40.317	1.60549	11	11	2.48	40.317	1.60549											
5000	2.60	38.459	1.58499	30	67.52	1.481	0.17058	10	38.19	2.618	0.41810	12	2.37	42.224	1.62556	12	12	2.37	42.224	1.62556											
5250	2.17	46.158	1.66424	40	67.00	1.492	0.17393	20	37.89	2.639	0.42144	13	2.26	44.221	1.64563	13	13	2.26	44.221	1.64563											
5500	1.81	55.398	1.74349	50	66.49	1.504	0.17727	30	37.60	2.659	0.42479	14	2.16	46.312	1.66570	14	14	2.16	46.312	1.66570											
5750	1.50	66.488	1.82274	9	0	65.98	1.515	0.18062	40	37.31	2.679	0.42813	15	2.06	48.502	1.68577	15	15	2.06	48.502	1.68577										
6000	1.25	79.798	1.90199	10	65.47	1.527	0.18396	50	37.03	2.700	0.43148	16	1.97	50.796	1.70584	16	16	1.97	50.796	1.70584											
6250	1.04	95.773	1.98124	20	64.97	1.539	0.18731	10	36.74	2.721	0.43482	17	1.88	53.199	1.72591	17	17	1.88	53.199	1.72591											
6500	0.87	114.945	2.06049	30	64.47	1.551	0.19065	20	36.46	2.742	0.43817	18	1.79	55.714	1.74597	18	18	1.79	55.714	1.74597											
6750	0.72	137.956	2.13974	40	63.97	1.563	0.19400	30	36.18	2.763	0.44151	19	1.71	58.349	1.76604	19	19	1.71	58.349	1.76604											
7000	0.60	165.573	2.21899	50	63.48	1.575	0.19734	40	35.90	2.785	0.44486	20	1.64	61.109	1.78611	20	20	1.64	61.109	1.78611											
7250	0.50	198.719	2.29824	10	63.00	1.587	0.20069	50	35.63	2.806	0.44820	21	1.56	63.999	1.80618	21	21	1.56	63.999	1.80618											
				20	62.51	1.599	0.20403	10	35.36	2.828	0.45155	22	1.49	67.026	1.82625	22	22	1.49	67.026	1.82625											
				30	62.03	1.612	0.20738	20	35.08	2.850	0.45489	23	1.42	70.196	1.84631	23	23	1.42	70.196	1.84631											
				40	61.56	1.624	0.21072	30	34.81	2.872	0.45823	24	1.36	73.515	1.86638	24	24	1.36	73.515	1.86638											
				50	61.08	1.637	0.21407	40	34.55	2.894	0.46158	25	1.30	76.992	1.88645	25	25	1.30	76.992	1.88645											
				11	0	60.15	1.662	0.22076	50	34.28	2.916	0.46492	26	1.24	80.634	1.90652	26	26	1.24	80.634	1.90652										
				10	59.69	1.675	0.22410	20	34.02	2.939	0.46827	4	1.18	84.447	1.92659	4	4	1.18	84.447	1.92659											
				20	59.23	1.688	0.22745	30	33.76	2.962	0.47161	1	1.13	88.440	1.94666	1	1	1.13	88.440	1.94666											
				30	58.78	1.701	0.23079	40	33.50	2.985	0.47496	2	1.08	92.623	1.96672	2	2	1.08	92.623	1.96672											
				40	58.33	1.714	0.23413	50	33.24	3.008	0.47830	3	1.03	97.003	1.98679	3	3	1.03	97.003	1.98679											
				50	57.88	1.727	0.23748	1	0	32.99	3.031	0.48165	4	0.98	101.594	2.00687	4	4	0.98	101.594	2.00687										
				12	0	57.43	1.741	0.24082	1	31.50	3.174	0.50172	5	0.94	106.398	2.02694	5	5	0.94	106.398	2.02694										
				10	56.99	1.754	0.24417	2	30.08	3.324	0.52179	6	0.90	111.430	2.04700	6	6	0.90	111.430	2.04700											
				20	56.56	1.768	0.24751	3	28.72	3.482	0.54185	7	0.86	116.701	2.06708	7	7	0.86	116.701	2.06708											
				30	56.12	1.781	0.25086	4	27.42	3.646	0.56192	8	0.82	122.219	2.08714	8	8	0.82	122.219	2.08714											
				40	55.69	1.795	0.25420	5	26.18	3.819	0.58199	9	0.78	128.000	2.10721	9	9	0.78	128.000	2.10721											
				50	55.27	1.809	0.25																								

Isotope Decay Tables **Phosphorus-32 - Sulphur-35 - Potassium-42 - Calcium-45**

d	h	N_t	N_t/N_0	$\log_{10} N_t/N_0$	d	h	N_t	N_t/N_0	$\log_{10} N_t/N_0$	d	h	N_t	N_t/N_0	$\log_{10} N_t/N_0$	d	h	N_t	N_t/N_0	$\log_{10} N_t/N_0$
Phosphorus-32 half-life 14.3 d					Potassium-42 half-life 12.4 h					Calcium-45 half-life 165 d									
0	160.00	1.000	0.00000		0	100.00	1.000	0.00000		0	100.00	1.000	0.00000		0	100.00	1.000	0.00000	
1	99.40	1.006	0.00263		10	85.03	1.000	0.00000		10	98.15	1.000	0.00000		10	98.15	1.000	0.00000	
2	68.80	1.012	0.00520		20	78.15	1.028	0.00809		20	96.15	1.038	0.01618		20	96.15	1.038	0.01618	
3	39.20	1.018	0.00777		30	72.47	1.078	0.02124		30	94.54	1.048	0.02013		30	94.54	1.048	0.02013	
4	9.91	1.025	0.01035		40	67.33	1.154	0.06168		40	92.96	1.057	0.02426		40	92.96	1.057	0.02426	
5	17.02	1.031	0.01316		50	62.07	1.259	0.10337		50	91.56	1.067	0.02832		50	91.56	1.067	0.02832	
6	16.43	1.037	0.01579		60	57.33	1.392	0.14237		60	90.22	1.077	0.03237		60	90.22	1.077	0.03237	
7	93.85	1.043	0.01847		70	52.94	1.561	0.19647		70	88.91	1.087	0.03642		70	88.91	1.087	0.03642	
8	93.27	1.050	0.02105		80	48.91	1.775	0.24713		80	87.61	1.097	0.04046		80	87.61	1.097	0.04046	
9	92.99	1.057	0.02358		90	45.16	2.045	0.31070		90	86.33	1.108	0.04450		90	86.33	1.108	0.04450	
10	88.99	1.064	0.02615		100	41.71	2.397	0.37974		100	85.03	1.119	0.04854		100	85.03	1.119	0.04854	
11	88.99	1.071	0.02872		110	38.52	2.811	0.44979		110	83.51	1.130	0.05258		110	83.51	1.130	0.05258	
12	90.76	1.078	0.03130		120	35.58	3.295	0.51783		120	82.00	1.142	0.05662		120	82.00	1.142	0.05662	
13	86.47	1.085	0.03388		130	32.86	3.862	0.58587		130	80.56	1.154	0.06066		130	80.56	1.154	0.06066	
14	81.40	1.135	0.06115		140	30.31	4.519	0.65392		140	79.15	1.166	0.06470		140	79.15	1.166	0.06470	
15	78.48	1.274	0.10526		150	28.03	5.367	0.73297		150	77.76	1.178	0.06874		150	77.76	1.178	0.06874	
16	76.60	1.306	0.11578		160	25.91	6.412	0.81201		160	76.41	1.190	0.07278		160	76.41	1.190	0.07278	
17	74.76	1.338	0.12631		170	24.00	7.691	0.89206		170	75.09	1.202	0.07682		170	75.09	1.202	0.07682	
18	72.97	1.370	0.13683		180	22.49	9.210	0.96311		180	73.76	1.214	0.08086		180	73.76	1.214	0.08086	
19	71.23	1.404	0.14736		190	21.12	10.981	1.03416		190	72.44	1.226	0.08490		190	72.44	1.226	0.08490	
20	69.54	1.438	0.15789		200	20.00	13.013	1.10521		200	71.12	1.238	0.08894		200	71.12	1.238	0.08894	
21	67.86	1.474	0.16841		210	19.05	15.343	1.17626		210	69.80	1.250	0.09298		210	69.80	1.250	0.09298	
22	66.23	1.510	0.17893		220	18.31	18.019	1.24731		220	68.48	1.262	0.09702		220	68.48	1.262	0.09702	
23	64.65	1.547	0.18945		230	17.74	21.000	1.31836		230	67.16	1.274	0.10106		230	67.16	1.274	0.10106	
24	63.13	1.583	0.19997		240	17.30	24.353	1.38941		240	65.84	1.286	0.10510		240	65.84	1.286	0.10510	
25	61.59	1.624	0.21051		250	16.96	28.147	1.45046		250	64.52	1.298	0.10914		250	64.52	1.298	0.10914	
26	60.11	1.664	0.22104		260	16.72	32.353	1.51151		260	63.20	1.310	0.11318		260	63.20	1.310	0.11318	
27	58.67	1.704	0.23156		270	16.58	36.959	1.57256		270	61.88	1.322	0.11722		270	61.88	1.322	0.11722	
28	57.27	1.746	0.24209		280	16.50	42.050	1.62361		280	60.56	1.334	0.12126		280	60.56	1.334	0.12126	
29	55.90	1.789	0.25261		290	16.46	47.629	1.67466		290	59.24	1.346	0.12530		290	59.24	1.346	0.12530	
30	54.56	1.833	0.26313		300	16.43	53.699	1.72571		300	57.92	1.358	0.12934		300	57.92	1.358	0.12934	
31	53.25	1.878	0.27366		310	16.41	60.170	1.77676		310	56.60	1.370	0.13338		310	56.60	1.370	0.13338	
32	51.98	1.924	0.28419		320	16.40	67.153	1.82781		320	55.28	1.382	0.13742		320	55.28	1.382	0.13742	
33	50.73	1.971	0.29472		330	16.40	74.659	1.87886		330	53.96	1.394	0.14146		330	53.96	1.394	0.14146	
34	49.52	2.019	0.30524		340	16.40	82.699	1.92991		340	52.64	1.406	0.14550		340	52.64	1.406	0.14550	
35	48.33	2.069	0.31577		350	16.40	91.284	1.98096		350	51.32	1.418	0.14954		350	51.32	1.418	0.14954	
36	47.17	2.120	0.32629		360	16.40	100.425	2.03201		360	50.00	1.430	0.15358		360	50.00	1.430	0.15358	
37	46.04	2.172	0.33682		370	16.40	110.134	2.08306		370	48.68	1.442	0.15762		370	48.68	1.442	0.15762	
38	44.87	2.226	0.34735		380	16.40	120.421	2.13411		380	47.36	1.454	0.16166		380	47.36	1.454	0.16166	
39	43.71	2.280	0.35787		390	16.40	131.297	2.18516		390	46.04	1.466	0.16570		390	46.04	1.466	0.16570	
40	42.56	2.335	0.36840		400	16.40	142.774	2.23621		400	44.72	1.478	0.16974		400	44.72	1.478	0.16974	
41	41.41	2.391	0.37893		410	16.40	154.862	2.28726		410	43.40	1.490	0.17378		410	43.40	1.490	0.17378	
42	40.26	2.447	0.38946		420	16.40	167.571	2.33831		420	42.08	1.502	0.17782		420	42.08	1.502	0.17782	
43	39.11	2.504	0.39999		430	16.40	180.902	2.38936		430	40.76	1.514	0.18186		430	40.76	1.514	0.18186	
44	37.93	2.563	0.41052		440	16.40	194.865	2.44041		440	39.44	1.526	0.18590		440	39.44	1.526	0.18590	
45	36.73	2.623	0.42105		450	16.40	209.470	2.49146		450	38.12	1.538	0.18994		450	38.12	1.538	0.18994	
46	35.53	2.684	0.43158		460	16.40	224.727	2.54251		460	36.80	1.550	0.19398		460	36.80	1.550	0.19398	
47	34.33	2.746	0.44211		470	16.40	240.646	2.59356		470	35.48	1.562	0.19802		470	35.48	1.562	0.19802	
48	33.13	2.809	0.45264		480	16.40	257.228	2.64461		480	34.16	1.574	0.20206		480	34.16	1.574	0.20206	
49	31.92	2.873	0.46317		490	16.40	274.483	2.69566		490	32.84	1.586	0.20610		490	32.84	1.586	0.20610	
50	30.71	2.938	0.47370		500	16.40	292.422	2.74671		500	31.52	1.598	0.21014		500	31.52	1.598	0.21014	
51	29.50	3.004	0.48423		510	16.40	311.056	2.79776		510	30.20	1.610	0.21418		510	30.20	1.610	0.21418	
52	28.29	3.071	0.49476		520	16.40	330.395	2.84881		520	28.88	1.622	0.21822		520	28.88	1.622	0.21822	
53	27.08	3.139	0.50529		530	16.40	350.449	2.89986		530	27.56	1.634	0.22226		530	27.56	1.634	0.22226	
54	25.87	3.208	0.51582		540	16.40	371.218	2.95091		540	26.24	1.646	0.22630		540	26.24	1.646	0.22630	
55	24.66	3.278	0.52635		550	16.40	392.703	3.00196		550	24.92	1.658	0.23034		550	24.92	1.658	0.23034	
56	23.45	3.349	0.53688		560	16.40	414.814	3.05301		560	23.60	1.670	0.23438		560	23.60	1.670	0.23438	
57	22.24	3.421	0.54741		570	16.40	437.551	3.10406		570	22.28	1.682	0.23842		570	22.28	1.682	0.23842	
58	21.03	3.494	0.55794		580	16.40	460.924	3.15511		580	20.96	1.694	0.24246		580	20.96	1.694	0.24246	
59	19.82	3.568	0.56847		590	16.40	484.933	3.20616		590	19.64	1.706	0.24650		590	19.64	1.706	0.24650	
60	18.61	3.643	0.57899		600	16.40	509.578	3.25721		600	18.32	1.718	0.25054		600	18.32	1.718	0.25054	
61	17.40	3.719	0.58952		610	16.40	534.859	3.30826		610	17.00	1.730	0.25458		610	17.00	1.730	0.25458	
62	16.19	3.796	0.60005		620	16.40	560.776	3.35931		620	15.68	1.742	0.25862		620	15.68	1.742	0.25862	
63	15.00	3.874	0.61058		630	16.40	587.330	3.41036		630	14.36	1.754	0.26266		630	14.36	1.754	0.26266	
64	13.81	3.953	0.62111		640	16.40	614.521	3.46141		640	13.04	1.766	0.26670		640	13.04	1.766	0.26670	
65	12.62	4.033	0.63164		650	16.40	642.350	3.51246		650	11.72	1.778	0.27074		650	11.72	1.778	0.27074	
66	11.43	4.114	0.64217		660	16.40	670.827	3.56351		660	10.40	1.790	0.27478		660	10.40	1.790	0.27478	
67	10.24	4.196	0.6527																

N_t		N_0/N_t	$\log_{10} N_0/N_t$	t			N_t	N_0/N_t	$\log_{10} N_0/N_t$	t			N_t	N_0/N_t	$\log_{10} N_0/N_t$
				d	h	min				d	h	min			
4.76	21.024	1.32271	16				9.45	10.587	1.02479	40			36.89	2.711	0.43314
4.28	23.352	1.36832	17				8.15	12.270	1.08884	41			35.98	2.780	0.44397
3.86	25.938	1.41393	18				7.03	14.220	1.15289	42			35.09	2.850	0.45480
3.47	28.810	1.45955	19				6.07	16.479	1.21693	43			34.23	2.922	0.46562
2.81	35.544	1.55077	20				5.24	19.098	1.28098	44			33.38	2.995	0.47645
2.28	43.852	1.64199	22				3.90	25.650	1.40908	45			32.56	3.071	0.48728
1.85	54.102	1.73321	24				2.90	34.449	1.53718	46			31.76	3.149	0.49811
1.50	66.747	1.82443	26				2.16	46.268	1.66528	47			30.98	3.228	0.50894
1.21	82.348	1.91565	28				1.61	62.141	1.79338	48			30.22	3.310	0.51977
0.98	101.596	2.00687	30				1.20	83.460	1.92148	49			29.47	3.393	0.53059
0.80	125.342	2.09810	32				0.89	112.092	2.04957	50			28.75	3.479	0.54142
0.65	154.639	2.18932	34				0.66	150.547	2.17767	51			28.04	3.567	0.55225
0.52	190.783	2.28054	36				0.49	202.195	2.30577	52			27.35	3.657	0.56308
Calcium-47															
half-life 4.7 d															
Chromium-51															
half-life 27.8 d															
Manganese-54															
half-life 314 d															
Manganese-52															
half-life 5.7 d															
Iron-59															
half-life 45 d															

[illegible]

t d	N_t	N_0/N_t	\log_{10} N_0/N_t	t d	N_t	N_0/N_t	\log_{10} N_0/N_t	t d	N_t	N_0/N_t	\log_{10} N_0/N_t	t d	N_t	N_0/N_t	\log_{10} N_0/N_t
Cobalt-60 half-life 5.26 y				2900	35.12	2.847	0.45440	7850	5.89	16.983	1.23003	12750	1.01	99.498	1.99781
0	100.00	1.000	0.00000	2950	34.50	2.899	0.46224	7900	5.78	17.293	1.23786	12800	0.99	101.309	2.00565
20	99.28	1.007	0.00313	3000	33.88	2.952	0.47007	7950	5.68	17.607	1.24570	12850	0.97	103.153	2.01348
40	98.57	1.015	0.00627	3050	33.27	3.005	0.47791	8000	5.58	17.928	1.25353	12900	0.95	105.031	2.02132
60	97.86	1.022	0.00940	3100	32.68	3.060	0.48574	8050	5.48	18.254	1.26136	12950	0.94	106.943	2.02915
80	97.15	1.029	0.01254	3150	32.09	3.116	0.49358	8100	5.38	18.587	1.26920	13000	0.92	108.890	2.03699
100	96.46	1.037	0.01567	3200	31.52	3.173	0.50141	8150	5.28	18.925	1.27703	13050	0.90	110.872	2.04482
120	95.76	1.044	0.01880	3250	30.96	3.230	0.50925	8200	5.19	19.269	1.28487	13100	0.89	112.890	2.05266
140	95.07	1.052	0.02194	3300	30.40	3.289	0.51708	8250	5.10	19.620	1.29270	13150	0.87	114.945	2.06049
160	94.39	1.059	0.02507	3350	29.86	3.349	0.52492	8300	5.01	19.977	1.30054	13200	0.85	117.037	2.06832
180	93.71	1.067	0.02820	3400	29.33	3.410	0.53275	8350	4.92	20.341	1.30837	13250	0.84	119.168	2.07616
200	93.04	1.075	0.03134	3450	28.80	3.472	0.54058	8400	4.83	20.711	1.31621	13300	0.82	121.337	2.08399
220	92.37	1.083	0.03447	3500	28.29	3.535	0.54842	8450	4.74	21.088	1.32404	13350	0.81	123.546	2.09183
240	91.71	1.090	0.03761	3550	27.78	3.600	0.55625	8500	4.66	21.472	1.33188	13400	0.79	125.795	2.09966
260	91.05	1.098	0.04074	3600	27.28	3.665	0.56409	8550	4.57	21.863	1.33971	13450	0.78	128.085	2.10750
280	90.39	1.106	0.04387	3650	26.76	3.732	0.57192	8600	4.49	22.261	1.34755	13500	0.77	130.416	2.11533
300	89.74	1.114	0.04701	3700	26.26	3.800	0.57976	8650	4.41	22.666	1.35538	13550	0.75	132.790	2.12317
320	89.10	1.122	0.05014	3750	25.85	3.869	0.58759	8700	4.33	23.079	1.36321	13600	0.74	135.208	2.13100
340	88.46	1.131	0.05328	3800	25.38	3.939	0.59543	8750	4.26	23.499	1.37105	13650	0.73	137.669	2.13884
360	87.82	1.139	0.05641	3850	24.93	4.011	0.60326	8800	4.18	23.927	1.37888	13700	0.71	140.175	2.14667
380	87.19	1.147	0.05954	3900	24.49	4.084	0.61110	8850	4.10	24.362	1.38672	13750	0.70	142.727	2.15451
400	86.56	1.155	0.06268	3950	24.05	4.158	0.61893	8900	4.03	24.806	1.39455	13800	0.69	145.323	2.16234
420	85.94	1.164	0.06581	4000	23.62	4.234	0.62677	8950	3.96	25.257	1.40239	13850	0.68	147.970	2.17017
440	85.32	1.172	0.06894	4050	23.20	4.311	0.63460	9000	3.89	25.717	1.41022	13900	0.66	150.664	2.17801
460	84.71	1.181	0.07208	4100	22.78	4.390	0.64243	9050	3.82	26.185	1.41806	13950	0.65	153.406	2.18584
480	84.10	1.189	0.07521	4150	22.37	4.470	0.65027	9100	3.75	26.662	1.42589	14000	0.64	156.199	2.19368
500	83.49	1.198	0.07835	4200	21.97	4.551	0.65810	9150	3.68	27.147	1.43373	14050	0.63	159.042	2.20151
520	82.89	1.206	0.08148	4250	21.58	4.634	0.66594	9200	3.62	27.641	1.44156	14100	0.62	161.937	2.20935
540	82.30	1.215	0.08461	4300	21.19	4.718	0.67377	9250	3.55	28.145	1.44939	14150	0.61	164.885	2.21718
560	81.71	1.224	0.08775	4350	20.82	4.804	0.68161	9300	3.49	28.657	1.45723	14200	0.60	167.887	2.22502
580	81.12	1.233	0.09088	4400	20.44	4.891	0.68944	9350	3.43	29.179	1.46506	14250	0.58	170.943	2.23285
600	80.54	1.242	0.09401	4450	20.08	4.981	0.69728	9400	3.37	29.710	1.47290	14300	0.57	174.055	2.24069
620	79.96	1.251	0.09715	4500	19.72	5.071	0.70511	9450	3.31	30.251	1.48073	14350	0.56	177.223	2.24852
640	79.38	1.260	0.10028	4550	19.37	5.164	0.71295	9500	3.25	30.801	1.48857	14400	0.55	180.449	2.25635
660	78.81	1.269	0.10342	4600	19.02	5.258	0.72078	9550	3.19	31.362	1.49640	14450	0.54	183.734	2.26419
680	78.24	1.278	0.10655	4650	18.68	5.353	0.72861	9600	3.13	31.933	1.50424	14500	0.53	187.078	2.27202
700	77.68	1.287	0.10968	4700	18.35	5.451	0.73645	9650	3.08	32.514	1.51207	14550	0.52	190.484	2.27986
720	77.12	1.297	0.11282	4750	18.02	5.550	0.74428	9700	3.02	33.106	1.51991	14600	0.52	193.951	2.28769
740	76.57	1.306	0.11595	4800	17.70	5.651	0.75212	9750	2.97	33.709	1.52774	14650	0.51	197.482	2.29553
760	76.02	1.315	0.11909	4850	17.38	5.754	0.75995	9800	2.91	34.322	1.53557	14700	0.50	201.077	2.30336
780	75.47	1.325	0.12222	4900	17.07	5.859	0.76779	9850	2.86	34.947	1.54341				
800	74.93	1.335	0.12535	4950	16.76	5.965	0.77562	9900	2.81	35.583	1.55124				
820	74.39	1.344	0.12849	5000	16.46	6.074	0.78346	9950	2.76	36.231	1.55908				
840	73.85	1.354	0.13162	5050	16.17	6.184	0.79129	10000	2.71	36.890	1.56691				
860	73.32	1.364	0.13475	5100	15.88	6.297	0.79913	10050	2.66	37.566	1.57475				
880	72.80	1.374	0.13789	5150	15.60	6.412	0.80696	10100	2.61	38.246	1.58258				
900	72.27	1.384	0.14102	5200	15.32	6.528	0.81479	10150	2.57	38.942	1.59042				
920	71.75	1.394	0.14416	5250	15.04	6.647	0.82263	10200	2.52	39.651	1.59825				
940	71.24	1.404	0.14729	5300	14.78	6.768	0.83046	10250	2.48	40.373	1.60609				
960	70.73	1.414	0.15042	5350	14.51	6.891	0.83830	10300	2.43	41.107	1.61392				
980	70.22	1.424	0.15356	5400	14.25	7.017	0.84613	10350	2.39	41.856	1.62175				
1000	69.71	1.434	0.15669	5450	14.00	7.144	0.85397	10400	2.35	42.618	1.62959				
1020	69.21	1.445	0.15983	5500	13.75	7.274	0.86180	10450	2.30	43.393	1.63742				
1040	68.71	1.455	0.16296	5550	13.50	7.407	0.86964	10500	2.26	44.183	1.64526				
1060	68.22	1.466	0.16609	5600	13.26	7.542	0.87747	10550	2.22	44.988	1.65309				
1080	67.73	1.476	0.16923	5650	13.02	7.679	0.88531	10600	2.18	45.807	1.66093				
1100	67.24	1.487	0.17236	5700	12.79	7.819	0.89314	10650	2.14	46.640	1.66876				
1120	66.76	1.498	0.17549	5750	12.56	7.961	0.90097	10700	2.11	47.489	1.67660				
1140	66.28	1.509	0.17863	5800	12.34	8.106	0.90881	10750	2.07	48.354	1.68443				
1160	65.80	1.520	0.18176	5850	12.12	8.254	0.91664	10800	2.03	49.234	1.69227				
1180	65.33	1.531	0.18490	5900	11.90	8.404	0.92448	10850	1.99	50.130	1.70010				
1200	64.86	1.542	0.18803	5950	11.69	8.557	0.93231	10900	1.96	51.043	1.70794				
1220	64.39	1.553	0.19116	6000	11.48	8.713	0.94015	10950	1.92	51.972	1.71577				
1240	63.92	1.564	0.19429	6050	11.27	8.871	0.94798	11000	1.89	52.918	1.72360				
1260	63.45	1.575	0.19742	6100	11.07	9.033	0.95582	11050	1.86	53.881	1.73144				
1280	62.98	1.586	0.20055	6150	10.87	9.197	0.96365	11100	1.82	54.862	1.73927				
1300	62.51	1.598	0.20368	6200	10.68	9.365	0.97149	11150	1.79	55.861	1.74711				
1320	62.04	1.609	0.20681	6250	10.49	9.535	0.97932	11200	1.76	56.878	1.75494				
1340	61.57	1.620	0.20994	6300	10.30	9.709	0.98716	11250	1.73	57.913	1.76278				
1360	61.10	1.631	0.21307	6350	10.12	9.885	0.99499	11300	1.70	58.967	1.77061				
1380	60.63	1.642	0.21620	6400	9.94	10.065	1.00282	11350	1.67	60.041	1.77845				
1400	60.16	1.653	0.21933	6450	9.76	10.248	1.01066	11400	1.64	61.134	1.78628				
1420	59.69	1.664	0.22246	6500	9.58	10.435	1.01849	11450	1.61	62.247	1.79412				
1440	59.22	1.675	0.22559	6550	9.41	10.625	1.02633	11500	1.58	63.380	1.80195				
1460	58.75	1.686	0.22872	6600	9.24	10.818	1.03416	11550	1.55	64.533	1.80978				
1480	58.28	1.697	0.23185	6650											

t d	h	N_t	N_t/N_0	$\log_{10} N_t/N_0$	t d	N_t	N_t/N_0	$\log_{10} N_t/N_0$	t d	N_t	N_t/N_0	$\log_{10} N_t/N_0$	t d	h	N_t	N_t/N_0	$\log_{10} N_t/N_0$
2	24.57	4.070	0.60956	600	18.31	5.460	0.73722	280	20.11	5.976	0.69660	8	0	85.50	1.170	0.06803	
3	23.28	4.295	0.63301	614	17.89	5.616	0.74950	290	18.99	5.263	0.72148	8	0	84.94	1.177	0.07486	
4	22.06	4.534	0.65645	620	17.31	5.778	0.76179	300	17.93	5.576	0.74636	9	0	84.39	1.185	0.07730	
5	20.90	4.785	0.67990	630	16.82	5.943	0.77408	310	16.93	5.905	0.77124	9	0	83.84	1.193	0.07653	
6	19.80	5.051	0.70334	640	16.35	6.114	0.78636	320	15.99	6.251	0.79612	20	0	83.30	1.201	0.07937	
7	18.76	5.331	0.72679	650	15.90	6.289	0.79865	330	15.10	6.622	0.82099	20	0	82.76	1.208	0.08220	
8	17.77	5.626	0.75024	660	15.45	6.470	0.81094	340	14.26	7.012	0.84587	20	0	82.22	1.216	0.08504	
9	16.84	5.933	0.77368	670	15.02	6.656	0.82322	350	13.47	7.426	0.87075	20	0	81.68	1.224	0.08787	
10	15.95	6.268	0.79712	680	14.60	6.847	0.83551	360	12.72	7.864	0.89563	40	0	81.15	1.232	0.09071	
11	15.12	6.616	0.82057	690	14.20	7.043	0.84780	370	12.01	8.327	0.92051	11	0	80.62	1.240	0.09354	
12	14.32	6.983	0.84401	700	13.80	7.245	0.86008	380	11.34	8.818	0.94539	11	0	80.10	1.248	0.09638	
13	12.18	8.210	0.91435	720	13.04	7.667	0.88466	390	10.71	9.338	0.97027	12	0	79.58	1.257	0.09921	
14	10.36	9.653	0.98468	740	12.32	8.113	0.90523	400	10.11	9.889	0.99514	12	0	79.06	1.265	0.10204	
15	8.85	11.351	1.05502	760	11.65	8.589	0.93380	410	9.55	10.472	1.02001	20	0	78.55	1.273	0.10488	
16	7.49	13.346	1.12535	780	11.01	9.085	0.95337	420	9.02	11.087	1.04490	40	0	78.03	1.281	0.10771	
17	6.37	15.692	1.19568	800	10.40	9.614	0.96895	430	8.52	11.743	1.06978	13	0	77.53	1.290	0.11055	
18	5.42	18.451	1.26602	820	9.83	10.174	1.00753	440	8.04	12.435	1.09466	13	0	77.02	1.298	0.11338	
19	4.61	21.695	1.33635	840	9.29	10.767	1.03210	450	7.59	13.169	1.11954	40	0	76.52	1.307	0.11622	
20	3.92	25.509	1.40669	860	8.78	11.394	1.05668	460	7.17	13.945	1.14442	14	0	76.02	1.315	0.11905	
21	3.33	29.993	1.47702	880	8.29	12.057	1.08125	470	6.77	14.767	1.16929	20	0	75.53	1.324	0.12189	
22	2.84	35.246	1.54736	900	7.84	12.755	1.10583	480	6.39	15.636	1.19417	40	0	75.04	1.333	0.12472	
23	2.41	41.466	1.61769	920	7.41	13.502	1.13040	490	6.04	16.560	1.21905	15	0	74.55	1.341	0.12756	
24	2.05	48.756	1.68803	940	7.00	14.288	1.15497	500	5.70	17.536	1.24393	20	0	74.06	1.350	0.13039	
25	1.74	57.327	1.75836	960	6.61	15.119	1.17955	510	5.39	18.570	1.26881	40	0	73.58	1.359	0.13322	
26	1.44	67.481	1.82869	980	6.25	16.000	1.20412	520	5.09	19.665	1.29369	16	0	73.10	1.368	0.13606	
27	1.26	79.255	1.89903	1000	5.91	16.931	1.22869	530	4.81	20.824	1.31857	20	0	72.63	1.377	0.13889	
28	1.07	91.189	1.96936	1020	5.60	17.909	1.25327	540	4.53	22.052	1.34345	40	0	72.16	1.386	0.14173	
29	0.96	105.511	2.03970	1040	5.31	18.933	1.27785	550	4.26	23.352	1.36832	17	0	71.69	1.395	0.14456	
30	0.78	123.451	2.11003	1060	5.04	20.024	1.30242	560	4.04	24.729	1.39320	20	0	71.22	1.404	0.14740	
31	0.61	145.434	2.18037	1080	4.78	21.275	1.32699	570	3.82	26.187	1.41808	40	0	70.76	1.413	0.15023	
32	0.56	178.115	2.25070	1100	4.53	22.684	1.35156	580	3.61	27.731	1.44296	18	0	70.30	1.423	0.15307	
33	0.56	178.115	2.25070	1120	4.29	24.251	1.37614	590	3.41	29.366	1.46784	20	0	69.84	1.432	0.15590	
34	0.56	178.115	2.25070	1140	4.06	25.987	1.40072	600	3.22	31.097	1.49272	40	0	69.38	1.441	0.15874	
35	0.56	178.115	2.25070	1160	3.84	27.891	1.42529	610	3.04	32.928	1.51760	19	0	68.93	1.451	0.16157	
36	0.56	178.115	2.25070	1180	3.63	29.964	1.44986	620	2.87	34.862	1.54247	20	0	68.48	1.460	0.16440	
37	0.56	178.115	2.25070	1200	3.43	32.191	1.47443	630	2.71	36.928	1.56735	40	0	68.04	1.470	0.16724	
38	0.56	178.115	2.25070	1220	3.23	34.567	1.49899	640	2.56	39.135	1.59223	20	0	67.60	1.479	0.17007	
39	0.56	178.115	2.25070	1240	3.04	37.104	1.52356	650	2.41	41.410	1.61711	20	0	67.16	1.489	0.17291	
40	0.56	178.115	2.25070	1260	2.86	39.821	1.54873	660	2.26	43.851	1.64199	40	0	66.72	1.499	0.17574	
41	0.56	178.115	2.25070	1280	2.69	42.747	1.57430	670	2.13	46.437	1.66687	21	0	66.29	1.509	0.17858	
42	0.56	178.115	2.25070	1300	2.53	45.887	1.60087	680	2.03	49.175	1.69175	20	0	65.85	1.519	0.18141	
43	0.56	178.115	2.25070	1320	2.39	49.251	1.62744	690	1.92	52.074	1.71662	40	0	65.43	1.528	0.18424	
44	0.56	178.115	2.25070	1340	2.25	52.851	1.65401	700	1.81	55.145	1.74150	22	0	65.00	1.538	0.18707	
45	0.56	178.115	2.25070	1360	2.13	56.687	1.68058	710	1.71	58.366	1.76638	20	0	64.58	1.549	0.18992	
46	0.56	178.115	2.25070	1380	2.02	60.769	1.70715	720	1.61	61.639	1.79126	40	0	64.16	1.559	0.19275	
47	0.56	178.115	2.25070	1400	1.91	65.209	1.73372	730	1.53	65.065	1.81614	23	0	63.74	1.569	0.19559	
48	0.56	178.115	2.25070	1420	1.81	69.914	1.76029	740	1.45	68.643	1.84102	20	0	63.32	1.579	0.19843	
49	0.56	178.115	2.25070	1440	1.71	74.904	1.78686	750	1.36	72.343	1.86590	40	0	62.91	1.589	0.20126	
50	0.56	178.115	2.25070	1460	1.61	80.189	1.81343	760	1.29	76.261	1.89077	1	0	62.50	1.599	0.20409	
51	0.56	178.115	2.25070	1480	1.51	85.770	1.84000	770	1.21	80.329	1.91565	20	0	62.09	1.609	0.20692	
52	0.56	178.115	2.25070	1500	1.41	91.659	1.86657	780	1.13	84.531	1.94053	40	0	61.69	1.619	0.20975	
53	0.56	178.115	2.25070	1520	1.31	97.958	1.89314	790	1.08	89.024	1.96541	1	0	61.29	1.629	0.21258	
54	0.56	178.115	2.25070	1540	1.21	104.667	1.91971	800	1.02	93.789	1.99029	20	0	60.89	1.639	0.21541	
55	0.56	178.115	2.25070	1560	1.11	111.796	1.94628	810	9.67	100.950	2.01517	40	0	60.50	1.649	0.21824	
56	0.56	178.115	2.25070	1580	1.01	119.345	1.97285	820	9.07	108.612	2.04005	20	0	60.10	1.659	0.22107	
57	0.56	178.115	2.25070	1600	0.91	127.314	2.00000	830	8.46	116.485	2.06493	40	0	59.71	1.669	0.22390	
58	0.56	178.115	2.25070	1620	0.81	135.713	2.02715	840	0.81	124.571	2.08980	20	0	59.32	1.679	0.22673	
59	0.56	178.115	2.25070	1640	0.71	144.542	2.05429	850	0.77	132.321	2.11468	40	0	58.93	1.689	0.22956	
60	0.56	178.115	2.25070	1660	0.61	153.901	2.08144	860	0.73	140.725	2.13956	20	0	58.54	1.699	0.23239	
61	0.56	178.115	2.25070	1680	0.51	163.800	2.10859	870	0.68	149.289	2.16444	40	0	58.15	1.709	0.23522	
62	0.56	178.115	2.25070	1700	0.41	174.259	2.13574	880	0.64	158.023	2.18932	20	0	57.76	1.719	0.23805	
63	0.56	178.115	2.25070	1720	0.31	185.288	2.16289	890	0.61	166.936	2.21420	40	0	57.37	1.729	0.24088	
64	0.56	178.115	2.25070	1740	0.21	196.897	2.19004	900	0.58	176.031	2.23908	20	0	56.98	1.739	0.24371	
65	0.56	178.115	2.25070	1760	0.11	209.096	2.21719	910	0.54	185.334	2.26395	40	0	56.59	1.749	0.24654	
66	0.56	178.115	2.25070	1780	0.01	221.895	2.24434	920	0.51	194.861	2.28883	20	0	56.20	1.759	0.24937	
67	0.56	178.115	2.25070	1800	0.01	235.294	2.27149					5	0	55.81	1.769	0.25220	
68	0.56	178.115	2.25070	1820	0.01	249.293	2.29864					20	0	55.42	1.779	0.25503	
69	0.56	178.115	2.25070	1840	0.01	263.892	2.32579					40	0	55.03	1.789	0.25786	
70	0.56	178.115	2.25070	1860	0.01	279.091	2.35294					20	0	54.64	1.799	0.26069	
71	0.56	178.115	2.25070	1880	0.01	294.890	2.38009					40	0	54.25	1.809	0.26352	
72	0.56	178.115	2.25070	1900	0.01	311.289	2.40724					20					

d		h	min.	N_t	N_0/N_t	$\log_{10} N_0/N_t$	t		N_t	N_0/N_t	$\log_{10} N_0/N_t$	t		N_t	N_0/N_t	$\log_{10} N_0/N_t$				
d							d					d								
2	0			39.07	2.560	0.40818	Krypton-85										10	87.29	1.146	0.05903
	1			38.31	2.610	0.41668	half-life 10.6 y										12	84.95	1.177	0.07083
	2			37.57	2.662	0.42519	0	100.00	1.000	0.00000	14	82.67	1.210	0.08264	2000	87.32	1.145	0.05887		
	3			36.84	2.714	0.43369	100	98.23	1.018	0.00778	16	80.46	1.243	0.09444	2200	86.15	1.161	0.06476		
	4			36.12	2.768	0.44219	200	96.48	1.036	0.01555	18	78.30	1.277	0.10625	2400	84.99	1.177	0.07065		
	5			35.42	2.823	0.45070	300	94.77	1.055	0.02333	20	76.20	1.312	0.11805	2600	83.84	1.193	0.07653		
	6			34.74	2.879	0.45920	400	93.09	1.074	0.03110	22	74.16	1.349	0.12986	2800	82.71	1.209	0.08242		
	7			34.06	2.936	0.46770	500	91.44	1.094	0.03888	24	72.17	1.386	0.14166	3000	81.60	1.225	0.08831		
	8			33.40	2.994	0.47621	600	89.81	1.113	0.04665	26	70.23	1.424	0.15347	3200	80.50	1.242	0.09419		
	9			32.76	3.053	0.48471	700	88.22	1.134	0.05443	28	68.35	1.463	0.16527	3400	79.42	1.259	0.10008		
	10	0		32.12	3.113	0.49321	800	86.66	1.154	0.06220	30	66.52	1.503	0.17708	3600	78.35	1.276	0.10597		
	11	0		31.50	3.175	0.50172	900	85.12	1.175	0.06998	32	64.73	1.545	0.18888	3800	77.29	1.294	0.11186		
	12	0		30.89	3.238	0.51022	1000	83.61	1.196	0.07775	34	63.00	1.587	0.20069	4000	76.25	1.311	0.11774		
	13	0		30.29	3.302	0.51873	1100	82.12	1.218	0.08553	36	61.31	1.631	0.21249	4200	75.23	1.329	0.12363		
	14	0		29.70	3.367	0.52723	1200	80.67	1.240	0.09331	38	59.66	1.676	0.22430	4400	74.21	1.347	0.12952		
	15	0		29.13	3.433	0.53573	1300	79.24	1.262	0.10108	40	58.06	1.722	0.23610	4600	73.21	1.366	0.13540		
	16	0		28.56	3.501	0.54424	1400	77.83	1.285	0.10886	42	56.51	1.770	0.24791	4800	72.23	1.384	0.14129		
	17	0		28.01	3.571	0.55274	1500	76.45	1.308	0.11663	44	54.99	1.818	0.25971	5000	71.26	1.403	0.14718		
	18	0		27.46	3.641	0.56124	1600	75.09	1.332	0.12441	46	53.52	1.869	0.27152	5200	70.30	1.423	0.15307		
	19	0		26.93	3.713	0.56975	1700	73.76	1.356	0.13218	48	52.08	1.920	0.28332	5400	69.35	1.442	0.15895		
3	0		26.41	3.787	0.57825	1800	72.45	1.380	0.13996	50	50.68	1.973	0.29513	5600	68.42	1.462	0.16484			
	1		25.90	3.861	0.58676	1900	71.17	1.405	0.14773	52	49.32	2.027	0.30693	5800	67.50	1.482	0.17073			
	2		25.39	3.938	0.59526	2000	69.90	1.431	0.15551	54	48.00	2.083	0.31874	6000	66.59	1.502	0.17661			
	3		24.90	4.016	0.60376	2100	68.66	1.456	0.16328	56	46.71	2.141	0.33054	6200	65.69	1.522	0.18250			
	4		24.42	4.095	0.61227	2200	67.44	1.483	0.17106	58	45.46	2.200	0.34235	6400	64.81	1.543	0.18839			
	5		23.95	4.176	0.62077	2300	66.25	1.510	0.17884	60	44.24	2.260	0.35415	6600	63.93	1.564	0.19427			
	6		23.48	4.259	0.62927	2400	65.07	1.537	0.18661	62	43.00	2.319	0.36596	6800	63.07	1.585	0.20016			
	7		23.03	4.343	0.63778	2500	63.90	1.563	0.19438	64	41.90	2.387	0.37776	7000	62.22	1.607	0.20605			
	8		22.58	4.429	0.64628	2600	62.78	1.593	0.20216	66	39.68	2.520	0.40137	7200	61.39	1.629	0.21194			
	9		22.14	4.516	0.65479	2700	61.66	1.620	0.21000	68	37.59	2.661	0.42499	7400	60.56	1.651	0.21782			
	10	0		21.71	4.606	0.66329	2800	60.57	1.651	0.21771	70	35.60	2.809	0.44860	7600	59.74	1.674	0.22371		
	11	0		21.29	4.697	0.67179	2900	59.50	1.682	0.22542	72	33.71	2.966	0.47221	7800	58.94	1.697	0.22960		
	12	0		20.88	4.790	0.68030	3000	58.44	1.711	0.23326	80	33.71	2.966	0.47221	8000	58.15	1.720	0.23548		
	13	0		20.47	4.884	0.68880	3100	57.39	1.743	0.24100	84	31.93	3.132	0.49582	8200	57.36	1.743	0.24137		
	14	0		20.08	4.981	0.69730	3200	56.39	1.773	0.24881	88	30.24	3.307	0.51943	8400	56.59	1.767	0.24726		
	15	0		19.69	5.079	0.70581	3300	55.40	1.806	0.25663	92	28.64	3.492	0.54304	8600	55.83	1.791	0.25315		
	16	0		19.31	5.180	0.71431	3400	54.40	1.838	0.26436	96	27.12	3.687	0.56665	8800	55.08	1.816	0.25903		
	17	0		18.93	5.282	0.72282	3500	52.49	1.905	0.27292	100	25.69	3.893	0.59026	9000	54.34	1.840	0.26492		
	18	0		18.56	5.387	0.73132	3600	50.64	1.975	0.28147	104	24.33	4.110	0.61387	9200	53.60	1.866	0.27081		
	19	0		18.20	5.493	0.73982	3800	48.86	2.047	0.31102	108	23.04	4.340	0.63748	9400	52.88	1.891	0.27669		
4	0		17.85	5.602	0.74833	4000	47.14	2.121	0.32657	112	21.82	4.582	0.66109	9600	52.17	1.917	0.28258			
	1		17.51	5.713	0.75683	4200	45.49	2.198	0.34212	116	20.67	4.838	0.68470	9800	51.47	1.943	0.28847			
	2		17.17	5.826	0.76533	4400	43.89	2.279	0.35767	120	19.57	5.109	0.70831	10000	50.77	1.969	0.29436			
	3		16.83	5.941	0.77384	4600	42.34	2.362	0.37322	124	18.54	5.394	0.73192	10200	50.09	1.996	0.30024			
	4		16.51	6.058	0.78234	4800	40.85	2.448	0.38877	128	17.56	5.695	0.75553	10400	49.42	2.024	0.30613			
	5		16.19	6.178	0.79084	5000	39.42	2.537	0.40432	132	16.63	6.014	0.77914	10600	48.75	2.051	0.31202			
	6		15.87	6.300	0.79935	5200	38.03	2.630	0.41987	136	15.75	6.350	0.80275	10800	48.09	2.079	0.31790			
	7		15.56	6.425	0.80785	5400	36.69	2.725	0.43542	140	14.92	6.704	0.82636	11000	47.45	2.108	0.32379			
	8	0		15.26	6.552	0.81636	5600	35.40	2.825	0.45098	150	13.02	7.680	0.88539	11200	46.81	2.136	0.32968		
	9	0		14.97	6.681	0.82486	5800	34.16	2.928	0.46653	160	11.37	8.799	0.94441	11400	46.18	2.166	0.33557		
	10	0		14.68	6.813	0.83336	6000	31.80	3.145	0.49763	170	9.92	10.079	1.00344	11600	45.56	2.195	0.34145		
	11	0		14.39	6.948	0.84187	6200	29.60	3.379	0.52873	180	8.66	11.547	1.06246	11800	44.94	2.225	0.34734		
	12	0		14.11	7.086	0.85037	6400	27.55	3.629	0.55983	190	7.56	13.228	1.12149	12000	44.34	2.255	0.35323		
	13	0		13.84	7.226	0.85887	6600	25.65	3.899	0.59093	200	6.60	15.154	1.18051	12200	43.74	2.286	0.35911		
	14	0		13.57	7.368	0.86738	6800	23.88	4.188	0.62203	210	5.76	17.360	1.23954	12400	43.15	2.317	0.36500		
	15	0		13.31	7.514	0.87588	7000	22.23	4.499	0.65314	220	5.03	19.887	1.29857	12600	42.57	2.349	0.37089		
	16	0		13.05	7.663	0.88439	7200	20.69	4.833	0.68424	230	4.39	22.782	1.35759	12800	42.00	2.381	0.37678		
	17	0		12.80	7.814	0.89289	7400	19.26	5.192	0.71534	240	3.83	26.099	1.41662	13000	41.43	2.414	0.38266		
	18	0		12.55	7.969	0.90139	7600	17.93	5.578	0.74644	250	3.34	29.898	1.47564	13200	40.87	2.447	0.38855		
	19	0																		

t d	N_t	N_t/N_0	\log_{10} N_t/N_0	t h	N_t	N_t/N_0	\log_{10} N_t/N_0	t min	N_t	N_t/N_0	\log_{10} N_t/N_0	t h	N_t	N_t/N_0	\log_{10} N_t/N_0		
Yttrium-90 half-life 64.2 h																	
30000	13.09	7.640	0.88307	0	100.00	1.000	0.00000	4	0	35.47	2.819	0.44014	17	0	1.22	81.864	1.91310
30500	12.65	7.903	0.89739	1	98.93	1.011	0.00469	5	1	35.09	2.890	0.45483	18	0	1.07	93.189	1.96936
31000	12.23	8.175	0.91250	2	97.66	1.022	0.00938	6	2	34.71	2.981	0.45352	19	0	0.94	106.079	2.02563
31500	11.83	8.457	0.92723	3	96.18	1.033	0.01407	7	3	34.34	3.072	0.48670	20	0	0.83	120.753	2.08190
32000	11.43	8.740	0.94194	4	94.74	1.044	0.01875	8	4	33.97	3.164	0.47358	21	0	0.73	137.457	2.13817
32500	11.05	9.050	0.95666	5	93.23	1.055	0.02344	9	5	33.61	3.256	0.48070	22	0	0.64	156.471	2.19443
33000	10.68	9.362	0.97137	6	91.75	1.067	0.02813	10	6	33.25	3.348	0.48782	23	0	0.56	178.115	2.25070
33500	10.33	9.695	0.98609	7	90.30	1.078	0.03282	11	7	32.89	3.440	0.49494	24	0	0.49	202.753	2.30697
34000	9.98	10.019	1.00081	8	88.86	1.089	0.03751	12	8	32.53	3.532	0.50206					
34500	9.65	10.364	1.01553	9	87.45	1.100	0.04220	13	9	32.18	3.624	0.50918					
35000	9.33	10.721	1.03025	10	86.07	1.111	0.04689	14	10	31.84	3.716	0.51630					
35500	9.02	11.091	1.04496	11	84.71	1.122	0.05158	15	11	31.50	3.808	0.52342					
36000	8.72	11.473	1.05968	12	83.38	1.133	0.05627	16	12	31.16	3.900	0.53054					
36500	8.43	11.859	1.07440	13	82.08	1.144	0.06096	17	13	30.83	3.992	0.53766					
37000	8.14	12.278	1.08912	14	80.80	1.155	0.06565	18	14	30.49	4.084	0.54478					
37500	7.87	12.701	1.10383	15	79.54	1.166	0.07033	19	15	30.16	4.176	0.55190					
38000	7.61	13.131	1.11855	16	78.30	1.177	0.07502	20	16	29.83	4.268	0.55902					
38500	7.36	13.572	1.13327	17	77.08	1.188	0.07971	21	17	29.52	4.360	0.56614					
39000	7.11	14.060	1.14799	18	75.89	1.199	0.08440	22	18	29.21	4.452	0.57326					
39500	6.88	14.545	1.16271	19	74.72	1.210	0.08909	23	19	28.92	4.544	0.58038					
40000	6.66	15.046	1.17742	20	73.58	1.221	0.09378	24	20	28.63	4.636	0.58750					
40500	6.42	15.565	1.19214	21	72.46	1.232	0.09847	25	21	28.35	4.728	0.59462					
41000	6.21	16.101	1.20686	22	71.36	1.243	0.10316	26	22	28.07	4.820	0.60174					
41500	6.00	16.656	1.22158	23	70.28	1.254	0.10785	27	23	27.80	4.912	0.60886					
42000	5.80	17.230	1.23629	24	69.22	1.265	0.11254	28	24	27.53	5.004	0.61598					
42500	5.61	17.824	1.25101	25	68.18	1.276	0.11723	29	25	27.27	5.096	0.62310					
43000	5.42	18.439	1.26573	26	67.16	1.287	0.12191	30	26	27.02	5.188	0.63022					
43500	5.24	19.074	1.28045	27	66.16	1.298	0.12660	31	27	26.77	5.280	0.63734					
44000	5.07	19.732	1.29517	28	65.18	1.309	0.13129	32	28	26.53	5.372	0.64446					
44500	4.90	20.412	1.30989	29	64.22	1.320	0.13598	33	29	26.30	5.464	0.65158					
45000	4.74	21.115	1.32460	30	63.28	1.331	0.14067	34	30	26.07	5.556	0.65870					
45500	4.58	21.843	1.33932	31	62.36	1.342	0.14536	35	31	25.85	5.648	0.66582					
46000	4.43	22.596	1.35404	32	61.46	1.353	0.15005	36	32	25.63	5.740	0.67294					
46500	4.28	23.375	1.36875	33	60.58	1.364	0.15474	37	33	25.42	5.832	0.68006					
47000	4.14	24.181	1.38347	34	59.72	1.375	0.15943	38	34	25.21	5.924	0.68718					
47500	4.00	25.014	1.39819	35	58.88	1.386	0.16411	39	35	25.01	6.016	0.69430					
48000	3.86	25.877	1.41291	36	58.06	1.397	0.16880	40	36	24.81	6.108	0.70142					
48500	3.74	26.769	1.42763	37	57.26	1.408	0.17349	41	37	24.62	6.200	0.70854					
49000	3.61	27.691	1.44235	38	56.48	1.419	0.17818	42	38	24.43	6.292	0.71566					
49500	3.49	28.646	1.45706	39	55.72	1.430	0.18287	43	39	24.25	6.384	0.72278					
50000	3.37	29.633	1.47178	40	55.00	1.441	0.18756	44	40	24.07	6.476	0.72990					
50500	3.26	30.655	1.48650	41	54.30	1.452	0.19225	45	41	23.90	6.568	0.73702					
51000	3.15	31.711	1.50121	42	53.62	1.463	0.19694	46	42	23.73	6.660	0.74414					
51500	3.05	32.804	1.51593	43	52.96	1.474	0.20163	47	43	23.57	6.752	0.75126					
52000	2.95	33.933	1.53065	44	52.32	1.485	0.20632	48	44	23.41	6.844	0.75838					
52500	2.85	35.105	1.54537	45	51.70	1.496	0.21101	49	45	23.26	6.936	0.76550					
53000	2.76	36.319	1.56009	46	51.10	1.507	0.21570	50	46	23.11	7.028	0.77262					
53500	2.66	37.567	1.57480	47	50.52	1.518	0.22039	51	47	22.97	7.120	0.77974					
54000	2.57	38.850	1.58952	48	50.00	1.529	0.22508	52	48	22.83	7.212	0.78686					
54500	2.47	40.201	1.60424	49	49.50	1.540	0.22977	53	49	22.70	7.304	0.79398					
55000	2.40	41.627	1.61896	50	49.02	1.551	0.23446	54	50	22.57	7.396	0.80110					
55500	2.32	43.130	1.63367	51	48.56	1.562	0.23915	55	51	22.45	7.488	0.80822					
56000	2.25	44.703	1.64839	52	48.12	1.573	0.24384	56	52	22.33	7.580	0.81534					
56500	2.18	46.351	1.66311	53	47.70	1.584	0.24853	57	53	22.22	7.672	0.82246					
57000	2.11	48.074	1.67783	54	47.30	1.595	0.25322	58	54	22.11	7.764	0.82958					
57500	2.03	49.266	1.69255	55	46.92	1.606	0.25791	59	55	22.01	7.856	0.83670					
58000	1.96	50.904	1.70726	56	46.56	1.617	0.26260	60	56	21.91	7.948	0.84382					
58500	1.90	52.721	1.72198	57	46.22	1.628	0.26729	61	57	21.81	8.040	0.85094					
59000	1.83	54.618	1.73670	58	45.89	1.639	0.27198	62	58	21.72	8.132	0.85806					
59500	1.77	56.415	1.75142	59	45.58	1.650	0.27667	63	59	21.63	8.224	0.86518					
60000	1.71	58.163	1.76613	60	45.28	1.661	0.28136	64	60	21.54	8.316	0.87230					
60500	1.66	60.374	1.78085	61	45.00	1.672	0.28605	65	61	21.45	8.408	0.87942					
61000	1.60	62.435	1.79557	62	44.74	1.683	0.29074	66	62	21.37	8.500	0.88654					
61500	1.55	64.604	1.81029	63	44.50	1.694	0.29543	67	63	21.29	8.592	0.89366					
62000	1.50	66.859	1.82501	64	44.28	1.705	0.30012	68	64	21.21	8.684	0.90078					
62500	1.45	69.139	1.83972	65	44.08	1.716	0.30481	69	65	21.13	8.776	0.90790					
63000	1.40	71.425	1.85444	66	43.89	1.727	0.30950	70	66	21.05	8.868	0.91502					
63500	1.36	73.884	1.86916	67	43.72	1.738	0.31419	71	67	20.97	8.960	0.92214					
64000	1.31	76.418	1.88388	68	43.56	1.749	0.31888	72	68	20.90	9.052	0.92926					
64500	1.26	79.017	1.89860	69	43.42	1.760	0.32357	73	69	20.83	9.144	0.93638					
65000	1.21	81.695	1.91331	70	43.28	1.771	0.32826	74	70	20.76	9.236	0.94350					
65500	1.14	84.729	1.92803	71	43.16	1.782	0.33295	75	71	20.69	9.328	0.95062					
66000	1.14	87.611	1.94275	72	43.05	1.793	0.33764	76	72	20.63	9.420	0.95774					
66500	1.07	91.670	1.95747	73	42.96	1.804	0.34233	77	73	20.57	9.512	0.96486					
67000	1.07	93.796	1.97218	74	42.88	1.815	0.34702	78	74	20.51	9.604	0.97198					
67500	1.03	97.029	1.98690	75	42.82	1.826	0.35171	79	75	20.45	9.696	0.97910					
68000	1.00	100.374	2.00162	76	42.77	1.837	0.35640	80	76	20.40	9.788	0.98622					
68500	0.96	103.833	2.01634	77	42.73	1.848	0.36109	81	77	20.35	9.880	0.99334				</	

Molybdenum-99					Technetium-99m					Technetium-99m					Tellurium-132				
d	h	min	N_t	N_0/N_t	$\log_{10} N_0/N_t$	d	h	min	N_t	N_0/N_t	$\log_{10} N_0/N_t$	d	h	min	N_t	N_0/N_t	$\log_{10} N_0/N_t$		
14	14	08	41.08	2.434	0.38640	13	0		3.96	25.224	1.40182	6	6		94.81	1.055	0.02316		
15	40.65		2.460	0.39089		12	12		3.50	28.558	1.45573	7	7		93.97	1.064	0.02702		
16	40.24		2.485	0.39538		14	0		3.09	32.333	1.50965	8	8		93.14	1.074	0.03087		
17	39.82		2.511	0.39988		12	12		2.73	36.607	1.56357	9	9		92.31	1.083	0.03473		
18	39.41		2.537	0.40437		15	0		2.41	41.446	1.61748	10	10		91.50	1.093	0.03859		
19	39.01		2.564	0.40886		12	12		2.13	46.924	1.67140	11	11		90.69	1.103	0.04245		
20	38.61		2.590	0.41336		16	0		1.88	53.127	1.72531	12	12		89.89	1.113	0.04631		
21	38.21		2.617	0.41785		12	12		1.66	60.149	1.77923	13	13		89.09	1.122	0.05017		
22	37.81		2.644	0.42234		17	0		1.47	68.100	1.83315	14	14		88.30	1.132	0.05403		
23	37.43		2.672	0.42684		12	12		1.30	77.101	1.88706	15	15		87.52	1.143	0.05789		
4	0		2.700	0.43133		18	0		1.15	87.293	1.94098	16	16		86.75	1.153	0.06175		
1	2		2.728	0.43582		19	0		1.01	98.831	1.99489	17	17		85.98	1.163	0.06561		
2	3		2.756	0.44031		12	12		0.89	111.895	2.04881	18	18		85.22	1.173	0.06947		
3	35.91		2.785	0.44481		12	12		0.79	126.685	2.10273	19	19		84.46	1.184	0.07333		
4	35.54		2.814	0.44930		20	0		0.70	143.431	2.15664	20	20		83.72	1.195	0.07719		
5	35.17		2.843	0.45379		12	12		0.62	162.389	2.21056	21	21		82.98	1.205	0.08105		
6	34.81		2.873	0.45829		21	0		0.54	183.854	2.26447	22	22		82.24	1.216	0.08491		
7	34.45		2.903	0.46278		12	12		0.48	208.156	2.31839	23	23		81.51	1.227	0.08877		
8	34.10		2.933	0.46727		Technetium-99m half-life 6 h													
9	33.75		2.963	0.47177		0	0		100.00	1.000	0.00000	1	0		80.79	1.238	0.09262		
10	33.40		2.994	0.47626		5	5		99.04	1.010	0.00418	1	1		80.08	1.249	0.09648		
11	33.06		3.025	0.48075		10	10		98.09	1.019	0.00836	2	2		79.37	1.260	0.10034		
12	32.72		3.057	0.48524		15	15		97.15	1.029	0.01254	3	3		78.67	1.271	0.10420		
13	32.38		3.088	0.48974		20	20		96.22	1.039	0.01672	4	4		77.97	1.283	0.10806		
14	32.05		3.121	0.49423		25	25		95.30	1.049	0.02090	5	5		77.28	1.294	0.11192		
15	31.72		3.153	0.49872		30	30		94.39	1.059	0.02509	6	6		76.60	1.306	0.11578		
16	31.39		3.186	0.50322		35	35		93.48	1.070	0.02927	7	7		75.92	1.317	0.11964		
17	31.07		3.219	0.50771		40	40		92.59	1.080	0.03345	8	8		75.25	1.329	0.12350		
18	30.75		3.252	0.51220		45	45		91.70	1.091	0.03763	9	9		74.58	1.341	0.12736		
19	30.43		3.286	0.51670		50	50		90.82	1.101	0.04181	10	10		73.92	1.353	0.13122		
20	30.12		3.320	0.52119		55	55		89.95	1.112	0.04599	11	11		73.27	1.365	0.13508		
21	29.81		3.355	0.52568		1	0		89.09	1.122	0.05017	12	12		72.62	1.377	0.13894		
22	29.50		3.390	0.53017		5	5		88.24	1.133	0.05435	13	13		71.98	1.389	0.14280		
23	29.20		3.425	0.53467		10	10		87.39	1.144	0.05853	14	14		71.34	1.402	0.14666		
5	0		2.890	0.53916		15	15		86.55	1.155	0.06271	15	15		70.71	1.414	0.15052		
1	2		2.860	0.54365		20	20		85.72	1.167	0.06690	16	16		70.08	1.427	0.15437		
2	3		2.830	0.54815		25	25		84.90	1.178	0.07108	17	17		69.46	1.440	0.15823		
3	28.01		3.570	0.55264		30	30		84.09	1.189	0.07526	18	18		68.85	1.452	0.16209		
4	27.72		3.607	0.55713		35	35		83.28	1.201	0.07944	19	19		68.24	1.465	0.16595		
5	27.44		3.644	0.56163		40	40		82.49	1.212	0.08362	20	20		67.64	1.478	0.16981		
6	27.16		3.682	0.56612		45	45		81.70	1.224	0.08780	21	21		67.04	1.492	0.17367		
7	26.88		3.721	0.57061		50	50		80.91	1.236	0.09198	22	22		66.45	1.505	0.17753		
8	26.60		3.759	0.57510		55	55		80.14	1.248	0.09616	23	23		65.86	1.518	0.18139		
9	26.33		3.798	0.57960		1	0		79.37	1.260	0.10034	2	0		65.28	1.532	0.18525		
10	26.06		3.838	0.58409		5	5		78.61	1.272	0.10452	1	1		64.70	1.546	0.18911		
11	25.79		3.878	0.58858		10	10		77.86	1.284	0.10871	2	2		64.13	1.559	0.19297		
12	25.52		3.918	0.59308		15	15		77.11	1.297	0.11289	3	3		63.56	1.573	0.19683		
13	25.26		3.959	0.59757		20	20		76.37	1.309	0.11707	4	4		63.00	1.587	0.20069		
14	25.00		4.000	0.60206		25	25		75.64	1.322	0.12125	5	5		62.44	1.602	0.20455		
15	24.74		4.042	0.60656		30	30		74.92	1.335	0.12543	6	6		61.89	1.616	0.20841		
16	24.49		4.084	0.61105		35	35		74.20	1.348	0.12961	7	7		61.34	1.630	0.21227		
17	24.24		4.126	0.61554		40	40		73.49	1.361	0.13379	8	8		60.80	1.645	0.21612		
18	23.99		4.169	0.62003		45	45		72.78	1.374	0.13797	9	9		60.26	1.660	0.21998		
19	23.74		4.212	0.62453		50	50		72.09	1.387	0.14215	10	10		59.73	1.674	0.22384		
20	23.50		4.256	0.62902		55	55		71.39	1.401	0.14633	11	11		59.20	1.689	0.22770		
21	23.25		4.300	0.63351		1	0		70.71	1.414	0.15052	12	12		58.67	1.704	0.23156		
22	23.01		4.345	0.63801		5	5		70.03	1.428	0.15470	13	13		58.15	1.720	0.23542		
23	22.78		4.390	0.64250		10	10		69.36	1.442	0.15888	14	14		57.64	1.735	0.23928		
6	0		2.254	0.64699		15	15		68.70	1.456	0.16306	15	15		57.13	1.750	0.24314		
1	1		2.231	0.6482	0.65149	20	20		68.04	1.470	0.16724	16	16		56.62	1.766	0.24700		
2	2		2.208	0.6529	0.65598	25	25		67.39	1.484	0.17142	17	17		56.12	1.782	0.25086		
3	3		2.185	0.6576	0.66047	30	30		66.74	1.498	0.17560	18	18		55.63	1.798	0.25472		
4	4		2.163	0.6623	0.66496	35	35		66.10	1.513	0.17978	19	19		55.13	1.814	0.25858		
5	5		2.141	0.6672	0.66946	40	40		65.47	1.527	0.18396	20	20		54.65	1.830	0.26244		
6	6		2.119	0.6720	0.67395	45	45		64.84	1.542	0.18814	21	21		54.16	1.846	0.26630		
7	7		2.097	0.6769	0.67844	50	50		64.22	1.557	0.19233	22	22		53.68	1.863	0.27016		
8	8		2.075	0.6819	0.68294	55	55		63.61	1.572	0.19651	23	23		53				

t d	h min	N_i	N_d/N_i	$\log_{10} N_d/N_i$	t d	N_i	N_d/N_i	$\log_{10} N_d/N_i$	t d	N_i	N_d/N_i	$\log_{10} N_d/N_i$	t d	h min	N_i	N_d/N_i	$\log_{10} N_d/N_i$
Iodine-125 half life 60 d																	
7	40.04	2.408	0.39752		124	23.87	4.189	0.62213	124	23.87	4.189	0.62213	4	0	70.83	1.412	
8	39.68	2.520	0.40137		126	23.33	4.287	0.63217	126	23.33	4.287	0.63217	4	0	70.07	1.427	
9	39.33	2.542	0.40523		128	22.79	4.387	0.64220	128	22.79	4.387	0.64220	4	0	69.32	1.443	
10	38.99	2.564	0.40909		130	22.27	4.490	0.65223	130	22.27	4.490	0.65223	4	0	68.58	1.458	
11	38.64	2.588	0.41295		132	21.76	4.595	0.66227	132	21.76	4.595	0.66227	4	0	67.84	1.474	
12	38.30	2.611	0.41681		134	21.27	4.702	0.67230	134	21.27	4.702	0.67230	4	0	67.12	1.490	
13	37.96	2.634	0.42067		136	20.78	4.812	0.68234	136	20.78	4.812	0.68234	4	0	66.40	1.506	
14	37.62	2.658	0.42453		138	20.30	4.925	0.69237	138	20.30	4.925	0.69237	4	0	65.68	1.522	
15	37.29	2.682	0.42839		140	19.84	5.040	0.70241	140	19.84	5.040	0.70241	5	0	64.98	1.539	
16	36.96	2.706	0.43225		142	19.39	5.157	0.71245	142	19.39	5.157	0.71245	5	0	64.29	1.556	
17	36.63	2.730	0.43611		144	18.93	5.275	0.72249	144	18.93	5.275	0.72249	5	0	63.60	1.572	
18	36.31	2.754	0.43997		146	18.48	5.395	0.73253	146	18.48	5.395	0.73253	5	0	62.91	1.589	
19	35.99	2.779	0.44383		148	18.03	5.515	0.74257	148	18.03	5.515	0.74257	5	0	62.24	1.607	
20	35.67	2.803	0.44769		150	17.58	5.637	0.75261	150	17.58	5.637	0.75261	5	0	61.57	1.624	
21	35.35	2.828	0.45155		152	17.13	5.760	0.76265	152	17.13	5.760	0.76265	5	0	60.91	1.642	
22	35.04	2.854	0.45541		154	16.68	5.884	0.77269	154	16.68	5.884	0.77269	5	0	60.26	1.659	
23	34.73	2.879	0.45927		156	16.23	6.009	0.78273	156	16.23	6.009	0.78273	5	0	59.61	1.677	
5	0	34.43	2.905	0.46312	158	15.78	6.134	0.79277	158	15.78	6.134	0.79277	5	0	58.96	1.696	
1	34.12	2.931	0.46698		160	15.33	6.260	0.80281	160	15.33	6.260	0.80281	5	0	58.34	1.714	
2	33.82	2.957	0.47084		162	14.88	6.387	0.81285	162	14.88	6.387	0.81285	5	0	57.72	1.733	
3	33.52	2.983	0.47470		164	14.43	6.515	0.82289	164	14.43	6.515	0.82289	5	0	57.10	1.751	
4	33.22	3.010	0.47856		166	13.98	6.643	0.83293	166	13.98	6.643	0.83293	5	0	56.49	1.770	
5	32.93	3.037	0.48242		168	13.53	6.771	0.84297	168	13.53	6.771	0.84297	5	0	55.89	1.789	
6	32.64	3.064	0.48628		170	13.08	6.900	0.85301	170	13.08	6.900	0.85301	5	0	55.29	1.808	
7	32.35	3.091	0.49014		172	12.63	7.028	0.86305	172	12.63	7.028	0.86305	5	0	54.69	1.828	
8	32.06	3.119	0.49400		174	12.18	7.157	0.87309	174	12.18	7.157	0.87309	5	0	54.09	1.848	
9	31.77	3.147	0.49786		176	11.73	7.286	0.88313	176	11.73	7.286	0.88313	5	0	53.52	1.868	
10	31.50	3.175	0.50172		178	11.28	7.415	0.89317	178	11.28	7.415	0.89317	5	0	52.92	1.889	
11	31.22	3.203	0.50558		180	10.83	7.544	0.90321	180	10.83	7.544	0.90321	5	0	52.32	1.909	
12	30.94	3.232	0.50944		182	10.38	7.673	0.91325	182	10.38	7.673	0.91325	5	0	51.72	1.930	
13	30.67	3.261	0.51330		184	9.93	7.802	0.92329	184	9.93	7.802	0.92329	5	0	51.12	1.951	
14	30.40	3.290	0.51716		186	9.48	7.931	0.93333	186	9.48	7.931	0.93333	5	0	50.52	1.972	
15	30.13	3.319	0.52102		188	9.03	8.060	0.94337	188	9.03	8.060	0.94337	5	0	49.92	1.993	
16	29.86	3.348	0.52488		190	8.58	8.189	0.95341	190	8.58	8.189	0.95341	5	0	49.32	2.014	
17	29.60	3.377	0.52873		192	8.13	8.318	0.96345	192	8.13	8.318	0.96345	5	0	48.72	2.035	
18	29.34	3.406	0.53259		194	7.68	8.447	0.97349	194	7.68	8.447	0.97349	5	0	48.12	2.056	
19	29.08	3.435	0.53645		196	7.23	8.576	0.98353	196	7.23	8.576	0.98353	5	0	47.52	2.077	
20	28.82	3.464	0.54031		198	6.78	8.705	0.99357	198	6.78	8.705	0.99357	5	0	46.92	2.098	
21	28.56	3.493	0.54417		200	6.33	8.834	1.00361	200	6.33	8.834	1.00361	5	0	46.32	2.119	
22	28.30	3.522	0.54803		202	5.88	8.963	1.01365	202	5.88	8.963	1.01365	5	0	45.72	2.140	
23	28.06	3.551	0.55189		204	5.43	9.092	1.02369	204	5.43	9.092	1.02369	5	0	45.12	2.161	
6	0	27.81	3.579	0.55575	206	4.98	9.221	1.03373	206	4.98	9.221	1.03373	5	0	44.52	2.182	
1	27.55	3.608	0.55961		208	4.53	9.350	1.04377	208	4.53	9.350	1.04377	5	0	43.92	2.203	
2	27.30	3.637	0.56347		210	4.08	9.479	1.05381	210	4.08	9.479	1.05381	5	0	43.32	2.224	
3	27.05	3.666	0.56733		212	3.63	9.608	1.06385	212	3.63	9.608	1.06385	5	0	42.72	2.245	
4	26.80	3.695	0.57119		214	3.18	9.737	1.07389	214	3.18	9.737	1.07389	5	0	42.12	2.266	
5	26.60	3.720	0.57505		216	2.73	9.866	1.08393	216	2.73	9.866	1.08393	5	0	41.52	2.287	
6	26.37	3.750	0.57891		218	2.28	9.995	1.09397	218	2.28	9.995	1.09397	5	0	40.92	2.308	
7	26.14	3.778	0.58277		220	1.83	10.124	1.10401	220	1.83	10.124	1.10401	5	0	40.32	2.329	
8	25.90	3.806	0.58663		222	1.38	10.253	1.11405	222	1.38	10.253	1.11405	5	0	39.72	2.350	
9	25.68	3.835	0.59049		224	0.93	10.382	1.12409	224	0.93	10.382	1.12409	5	0	39.12	2.371	
10	25.44	3.863	0.59435		226	0.48	10.511	1.13413	226	0.48	10.511	1.13413	5	0	38.52	2.392	
11	25.22	3.895	0.59820		228	0.03	10.640	1.14417	228	0.03	10.640	1.14417	5	0	37.92	2.413	
12	25.00	3.926	0.60206		230	0.00	10.769	1.15421	230	0.00	10.769	1.15421	5	0	37.32	2.434	
13	24.78	4.006	0.60592		232	0.00	10.898	1.16425	232	0.00	10.898	1.16425	5	0	36.72	2.455	
14	24.56	4.037	0.60978		234	0.00	11.027	1.17429	234	0.00	11.027	1.17429	5	0	36.12	2.476	
15	24.34	4.078	0.61364		236	0.00	11.156	1.18433	236	0.00	11.156	1.18433	5	0	35.52	2.497	
16	24.13	4.119	0.61750		238	0.00	11.285	1.19437	238	0.00	11.285	1.19437	5	0	34.92	2.518	
17	23.91	4.182	0.62136		240	0.00	11.414	1.20441	240	0.00	11.414	1.20441	5	0	34.32	2.539	
18	23.70	4.219	0.62522		242	0.00	11.543	1.21445	242	0.00	11.543	1.21445	5	0	33.72	2.560	
19	23.49	4.257	0.62908		244	0.00	11.672	1.22449	244	0.00	11.672	1.22449	5	0	33.12	2.581	
20	23.28	4.295	0.63294		246	0.00	11.801	1.23453	246	0.00	11.801	1.23453	5	0	32.52	2.602	
21	23.08	4.333	0.63680		248	0.00	11.930	1.24457	248	0.00	11.930	1.24457	5	0	31.92	2.623	
22	22.87	4.372	0.64066		250	0.00	12.059	1.25461	250	0.00	12.059	1.25461	5	0	31.32	2.644	
23	22.67	4.411	0.64452		252	0.00	12.188	1.26465	252	0.00	12.188	1.26465	5	0	30.72	2.665	
7	0	22.47	4.450	0.64837	254	0.00	12.317	1.27469	254	0.00	12.317	1.27469	5	0	30.12	2.686	
8	22.30	4.489	0.65223		256	0.00	12.446	1.28473	256	0.00	12.446	1.28473	5	0	29.52	2.707	
9	22.13	4.528	0.65609		258	0.00	12.575	1.29477	258	0.00	12.575	1.29477	5	0	28.92	2.728	
10	21.96	4.567	0.65995		260	0.00	12.704	1.30481	260	0.00	12.704	1.30481	5	0	28.32	2.749	
11	21.79	4.606	0.66381		262	0.00	12.833	1.31485	262	0.00	12.833	1.31485	5	0	27.72	2.770	
12	21.62	4.645	0.66767		264	0.00	12.962	1.32489	264	0.00	12.962	1.32489	5	0	27.12	2.791	
13	21.45	4.684	0.67153		266	0.00	13.091	1.33493	266	0.00	13.091	1.33493	5	0	26.52	2.812	
14	21.2																

Iodine-132						Caesium-137					
half-life 2.3 h						half-life 30 y					
d	h	min	N _t	N ₀ /N _t	log ₁₀ N ₀ /N _t	d	h	min	N _t	N ₀ /N _t	log ₁₀ N ₀ /N _t
1						2					
0	100.00	1.000	0.00000			0	100.00	1.000	0.00000		
2	99.00	1.010	0.00436			100	99.37	1.006	0.00275		
4	98.01	1.020	0.00873			200	98.74	1.012	0.00550		
6	97.03	1.031	0.01309			300	98.12	1.019	0.00824		
8	96.06	1.041	0.01745			400	97.50	1.025	0.01099		
10	95.10	1.052	0.02181			500	96.89	1.032	0.01374		
12	94.15	1.062	0.02618			600	96.28	1.038	0.01648		
14	93.21	1.073	0.03054			700	95.67	1.045	0.01923		
16	92.28	1.084	0.03490			800	95.07	1.051	0.02198		
18	91.36	1.095	0.03926			900	94.47	1.058	0.02473		
20	90.44	1.106	0.04363			1000	93.87	1.065	0.02747		
22	89.54	1.117	0.04799			1100	93.28	1.072	0.03022		
24	88.64	1.128	0.05235			1200	92.69	1.078	0.03297		
26	87.76	1.140	0.05672			1300	92.11	1.085	0.03572		
28	86.88	1.151	0.06108			1400	91.52	1.092	0.03847		
30	86.01	1.163	0.06544			1500	90.95	1.099	0.04121		
32	85.15	1.174	0.06980			1600	90.37	1.106	0.04396		
34	84.30	1.186	0.07417			1700	89.80	1.113	0.04670		
36	83.46	1.198	0.07853			1800	89.24	1.120	0.04945		
38	82.62	1.210	0.08289			1900	88.67	1.127	0.05220		
40	81.80	1.223	0.08726			2000	88.12	1.134	0.05495		
42	80.98	1.235	0.09162			2200	87.01	1.149	0.06044		
44	80.17	1.247	0.09598			2400	85.91	1.163	0.06594		
46	79.37	1.260	0.10034			2600	84.83	1.178	0.07143		
48	78.58	1.273	0.10471			2800	83.77	1.193	0.07693		
50	77.79	1.285	0.10907			3000	82.71	1.208	0.08242		
52	77.01	1.298	0.11343			3200	81.67	1.224	0.08792		
54	76.24	1.312	0.11779			3400	80.65	1.239	0.09341		
56	75.48	1.325	0.12216			3600	79.63	1.255	0.09890		
58	74.73	1.338	0.12652			3800	78.63	1.271	0.10440		
2						3					
0	73.98	1.352	0.13088			4000	77.64	1.287	0.10989		
2	73.24	1.365	0.13525			4200	76.67	1.304	0.11539		
4	72.51	1.379	0.13961			4400	75.70	1.320	0.12088		
6	71.78	1.393	0.14397			4600	74.75	1.337	0.12638		
8	71.07	1.407	0.14833			4800	73.81	1.354	0.13187		
10	70.36	1.421	0.15270			5000	72.88	1.372	0.13737		
12	69.65	1.436	0.15706			5200	71.97	1.389	0.14286		
14	68.96	1.450	0.16142			5400	71.06	1.407	0.14836		
16	68.27	1.465	0.16579			5600	70.17	1.425	0.15385		
18	67.59	1.480	0.17015			5800	69.29	1.443	0.15935		
20	66.91	1.495	0.17451			6000	68.42	1.461	0.16484		
22	66.24	1.510	0.17887			6200	67.56	1.480	0.17033		
24	65.58	1.525	0.18323			6400	66.71	1.499	0.17583		
26	64.92	1.540	0.18760			6600	65.87	1.518	0.18132		
28	64.27	1.555	0.19196			6800	65.04	1.537	0.18682		
30	63.63	1.572	0.19632			7000	64.22	1.557	0.19231		
32	63.00	1.587	0.20069			7200	63.42	1.576	0.19781		
34	62.37	1.603	0.20505			7400	62.62	1.596	0.20330		
36	61.74	1.620	0.20941			7600	61.83	1.617	0.20880		
38	61.13	1.636	0.21378			7800	61.05	1.637	0.21429		
40	60.51	1.652	0.21814			8000	60.29	1.658	0.21979		
42	59.91	1.669	0.22250			8200	59.53	1.679	0.22528		
44	59.31	1.686	0.22686			8400	58.78	1.701	0.23078		
46	58.72	1.703	0.23123			8600	58.04	1.722	0.23627		
48	58.13	1.720	0.23559			8800	57.31	1.744	0.24177		
50	57.55	1.738	0.23995			9000	56.59	1.767	0.24726		
52	56.98	1.755	0.24432			9200	55.88	1.789	0.25275		
54	56.41	1.773	0.24868			9400	55.18	1.812	0.25825		
56	55.84	1.791	0.25304			9600	54.48	1.835	0.26374		
58	55.28	1.809	0.25740			9800	53.80	1.858	0.26924		
3						4					
0	54.73	1.827	0.26177			10000	53.12	1.882	0.27473		
2	54.18	1.846	0.26613			10200	52.45	1.906	0.28023		
4	53.64	1.864	0.27049			10400	51.79	1.930	0.28572		
6	53.11	1.883	0.27485			10600	51.14	1.955	0.29122		
8	52.58	1.902	0.27922			10800	50.50	1.980	0.29671		
10	52.05	1.921	0.28358			11000	49.86	2.005	0.30221		
12	51.53	1.941	0.28794			11200	49.24	2.030	0.30770		
14	51.01	1.960	0.29231			11400	48.62	2.056	0.31320		
16	50.50	1.980	0.29667			11600	48.01	2.083	0.31869		
18	50.00	2.000	0.30103			11800	47.40	2.109	0.32419		
20	49.50	2.020	0.30539			12000	46.81	2.136	0.32968		
22	49.01	2.041	0.30976			12200	46.22	2.163	0.33517		
24	48.52	2.061	0.31412								
26	48.03	2.082	0.31848								
28	47.55	2.103	0.32285								
30	47.08	2.124	0.32721								
32	46.60	2.146	0.33157								
34	46.14	2.167	0.33593								
36	45.68	2.189	0.34030								
38	45.22	2.211	0.34466								
40	44.77	2.234	0.34902								
42	44.36	2.259	0.35393								
44	43.96	2.284	0.35884								
46	43.57	2.309	0.36375								
48	43.18	2.334	0.36866								
50	42.79	2.359	0.37357								
52	42.40	2.384	0.37848								
54	42.01	2.409	0.38339								
56	41.62	2.434	0.38830								
58	41.23	2.459	0.39321								
60	40.84	2.484	0.39812								
62	40.45	2.509	0.40303								
64	40.06	2.534	0.40794								
66	39.67	2.559	0.41285								
68	39.28	2.584	0.41776								
70	38.89	2.609	0.42267								
72	38.50	2.634	0.42758								
74	38.11	2.659	0.43249								
76	37.72	2.684	0.43740								
78	37.33	2.709	0.44231								
80	36.94	2.734	0.44722								
82	36.55	2.759	0.45213								
84	36.16	2.784	0.45704								
86	35.77	2.809	0.46195								
88	35.38	2.834	0.46686								
90	34.99	2.859	0.47177								
92	34.60	2.884	0.47668								
94	34.21	2.909	0.48159								
96	33.82	2.934	0.48650								
98	33.43	2.959	0.49141								
100	33.04	2.984	0.49632								

t d	N_t/N_0	$\log_{10} N_t/N_0$	t d	N_t	N_t/N_0	$\log_{10} N_t/N_0$	t h	N_t/N_0	$\log_{10} N_t/N_0$	t h	N_t/N_0	$\log_{10} N_t/N_0$	t h	N_t/N_0	$\log_{10} N_t/N_0$		
56000	2.89	34.554	153850	56	59.18	1.690	0.22781	22	79.03	1.285	0.10229	5	0	27.70	3.609	0.55746	
56500	2.90	34.564	153214	58	58.08	1.722	0.23594	23	78.19	1.275	0.10685	6	1	27.84	3.618	0.55934	
57000	2.73	36.810	156508	60	57.01	1.754	0.24308	1	0	77.36	1.292	0.11149	18	24.37	4.101	0.61321	
57500	2.62	37.993	157971	62	56.29	1.828	0.26035	2	1	76.52	1.306	0.12154	19	22.85	4.376	0.64108	
58000	2.55	39.214	159345	64	55.89	1.913	0.27662	3	2	75.72	1.320	0.12678	6	0	21.43	4.666	0.68096
58500	2.47	40.474	160719	72	50.95	1.963	0.29290	4	3	74.92	1.334	0.13245	6	0	20.10	4.955	0.69683
59000	2.41	41.775	162092	76	49.07	2.038	0.30917	5	4	74.12	1.349	0.13808	12	18.85	5.305	0.72470	
59500	2.32	43.117	163466	80	47.27	2.116	0.32544	6	5	73.33	1.363	0.14372	18	17.68	5.566	0.75257	
60000	2.25	44.503	164840	84	45.53	2.196	0.34171	7	6	72.55	1.378	0.14937	7	0	16.58	6.031	0.78045
60500	2.18	45.933	166213	88	43.85	2.280	0.35799	7	7	71.78	1.393	0.15461	12	15.55	6.431	0.80832	
61000	2.11	47.409	167587	92	42.24	2.367	0.37428	8	8	71.01	1.408	0.16066	12	14.58	6.857	0.83619	
61500	2.04	48.933	168960	96	40.69	2.458	0.39053	9	9	70.26	1.423	0.15330	18	15.48	7.312	0.86406	
62000	1.98	50.505	170334	100	39.19	2.552	0.40680	10	10	69.51	1.438	0.15795	8	0	12.83	7.797	0.89194
62500	1.92	52.128	171708	104	37.75	2.649	0.42307	11	11	68.77	1.454	0.16259	8	0	12.03	8.313	0.91981
63000	1.86	53.803	173081	108	36.36	2.750	0.43934	12	12	68.04	1.469	0.16724	12	11.28	8.865	0.94768	
63500	1.80	55.533	174455	112	35.03	2.854	0.45561	13	13	67.32	1.485	0.17188	18	10.98	9.452	0.97555	
64000	1.74	57.317	175829	116	33.74	2.964	0.47189	14	14	66.60	1.501	0.17653	9	0	9.92	10.076	1.00345
64500	1.69	59.159	177202	120	32.50	3.077	0.48816	15	15	65.89	1.517	0.18118	6	0	9.30	10.747	1.03131
65000	1.64	61.060	178576	124	31.30	3.195	0.50443	16	16	65.19	1.535	0.18582	12	8.73	11.459	1.05918	
65500	1.59	63.022	179950	128	30.15	3.317	0.52070	17	17	64.50	1.550	0.19047	18	8.18	12.219	1.08705	
66000	1.54	65.047	181323	132	29.04	3.443	0.53697	18	18	63.81	1.567	0.19511	10	0	7.67	13.029	1.11493
66500	1.49	67.137	182697	136	27.97	3.575	0.55325	19	19	63.15	1.584	0.19976	6	0	7.23	13.893	1.14280
67000	1.44	69.295	184071	140	26.95	3.708	0.56952	20	20	62.48	1.601	0.20440	12	6.33	15.795	1.19585	
67500	1.40	71.522	185444	144	25.98	3.841	0.58579	21	21	61.79	1.618	0.20905	18	0	5.94	16.842	1.22642
68000	1.35	73.820	186818	148	25.06	3.974	0.60206	22	22	61.14	1.635	0.21369	11	0	5.57	17.959	1.25420
68500	1.31	76.192	188191	152	24.08	4.113	0.61833	23	23	60.49	1.653	0.21834	12	0	5.22	19.169	1.28217
69000	1.27	78.641	189565	156	23.19	4.251	0.63461	2	0	59.84	1.671	0.22299	18	4.90	20.419	1.31004	
69500	1.23	81.166	190939	160	22.34	4.476	0.65088	1	1	59.21	1.689	0.22763	12	0	4.59	21.722	1.33791
70000	1.19	83.776	192312	170	20.34	4.915	0.69156	2	2	58.58	1.707	0.23228	12	0	4.31	22.751	1.36578
70500	1.12	86.468	193686	180	18.35	5.398	0.73224	3	3	57.95	1.725	0.23692	12	0	4.04	23.781	1.39365
71000	1.09	89.246	195059	190	16.87	5.928	0.77292	4	4	57.34	1.744	0.24157	12	0	3.79	24.812	1.42152
71500	1.02	92.114	196433	200	15.36	6.501	0.81360	5	5	56.73	1.762	0.24621	18	3.79	26.995	1.43363	
72000	1.05	95.074	197806	210	13.99	7.140	0.85428	6	6	56.12	1.781	0.25086	13	0	3.55	28.145	1.44940
72500	1.02	98.129	199180	220	12.74	7.852	0.89496	7	7	55.53	1.800	0.25550	6	0	3.33	30.010	1.47728
73000	0.99	101.285	200555	230	11.60	8.623	0.93564	8	8	54.94	1.820	0.26015	12	0	3.13	32.000	1.50515
73500	0.96	104.549	201929	240	10.56	9.469	0.97632	9	9	54.35	1.840	0.26480	12	0	2.93	34.121	1.53302
74000	0.93	107.909	203302	250	9.62	10.399	1.01700	10	10	53.77	1.859	0.26944	6	0	2.75	36.382	1.56090
74500	0.90	111.367	204676	260	8.76	11.420	1.05768	11	11	53.20	1.879	0.27409	12	0	2.58	38.785	1.58877
75000	0.87	114.946	206050	270	7.97	12.542	1.09836	12	12	52.63	1.899	0.27875	18	0	2.43	41.365	1.61664
75500	0.82	122.452	207927	280	7.26	13.773	1.15004	13	13	52.07	1.920	0.28338	18	0	2.27	44.107	1.64452
76000	0.77	130.449	211544	290	6.61	15.126	1.19792	14	14	51.52	1.940	0.28802	15	0	2.13	47.051	1.67239
76500	0.73	138.968	214292	300	6.02	16.611	1.24209	15	15	50.97	1.961	0.29267	6	0	1.99	50.148	1.70026
77000	0.68	148.042	217039	310	5.48	18.242	1.29108	16	16	50.43	1.982	0.29731	12	0	1.87	53.475	1.72813
77500	0.63	157.711	219786	320	4.99	20.033	1.30176	17	17	49.89	2.004	0.30196	18	0	1.75	57.071	1.75601
78000	0.60	168.010	222534	330	4.55	22.001	1.34244	18	18	49.36	2.025	0.30661	16	0	1.64	60.996	1.78388
78500	0.56	178.980	225281	340	4.14	24.161	1.38312	19	19	48.84	2.047	0.31125	6	0	1.54	64.826	1.81175
79000	0.52	190.668	228028	350	3.77	26.554	1.42380	20	20	48.32	2.069	0.31590	12	0	1.45	69.125	1.83963
79500	0.47	203.119	230775	360	3.45	29.182	1.46448	21	21	47.80	2.091	0.32054	18	0	1.36	73.735	1.86750
80000	0.46	216.354	233522	370	3.12	32.060	1.50516	22	22	47.29	2.113	0.32518	17	0	1.27	78.900	1.89537
80500	0.43	230.515	236270	380	2.85	35.143	1.54584	23	23	46.79	2.137	0.32983	12	0	1.19	83.799	1.92324
81000	0.41	245.567	239017	390	2.59	38.594	1.58652	4	0	46.29	2.160	0.33448	6	0	1.11	89.553	1.95111
81500	0.39	261.602	241764	400	2.36	42.385	1.62720	5	1	45.80	2.181	0.33912	18	0	1.05	95.276	1.97899
82000	0.36	278.691	244511	410	2.15	46.454	1.66788	6	2	45.31	2.206	0.34377	18	0	0.98	101.594	2.00686
82500	0.34	296.882	247258	420	1.96	50.823	1.70856	7	3	44.83	2.230	0.34841	6	0	0.92	108.228	2.03474
83000	0.32	316.275	250005	430	1.78	55.435	1.74924	8	4	44.35	2.256	0.35306	12	0	0.87	115.508	2.06261
83500	0.30	336.927	252752	440	1.62	60.467	1.78992	9	5	43.88	2.282	0.35771	18	0	0.81	123.564	2.09049
84000	0.28	358.937	255500	450	1.48	67.701	1.85060	6	4	43.42	2.303	0.36235	17	0	0.76	131.328	2.11836
84500	0.26	382.365	258248	460	1.35	74.349	1.91128	7	5	42.95	2.324	0.36700	6	0	0.71	140.034	2.14624
85000	0.25	407.344	260995	470	1.23	81.490	1.97195	8	6	42.50	2.353	0.37165	12	0	0.67	148.741	2.17411
85500	0.23	434.111	263742	480	1.12	87.667	1.99263	9	7	42.04	2.378	0.37629	18	0	0.65	159.212	2.20198
86000	0.22	462.278	266490	490	1.02	94.122	1.99331	10	8	41.59	2.402	0.38093	6	0	0.59	169.767	2.22986
86500	0.20	492.645	269238	500	0.92	100.842	2.03399	11	9	41.15	2.427	0.38558	20	0	0.16	178.782	2.25773
87000	0.19	524.631	271985	510	0.83	118.761	2.07467	12	10	40.72	2.455	0.39022	25	0	0.05	221.900	3.34470
100000	0.18	558.877	274732	520	0.77	130.420	2.15535	13	11	39.86	2.509	0.39952	30	0	0.01	298.720	3.90277
				530	0.68	157.295	2.19671	14	12	39.43	2.536	0.40416					
				540	0.61	189.733	2.27807	15	13	38.90	2.566	0.40881					
				550	0.48	208.331	2.31875	16	14	38.40	2.596	0.41345					
								17	15	37.91	2.618	0.41810					
								18	16	37.48	2.644	0.42274					
								19	17	37.08	2.675	0.42739					
								20	18								

d	h	min	N_t	N_0/N_t	$\log_{10} N_0/N_t$	d	h	min	N_t	N_0/N_t	$\log_{10} N_0/N_t$	d	h	min	N_t	N_0/N_t	$\log_{10} N_0/N_t$	d	h	min	N_t	N_0/N_t	$\log_{10} N_0/N_t$				
4	5		74.19	1.348	0.12967	6	7		26.09	3.833	0.58354	6	0		91.53	1.093	0.03843	126			15.59	6.412	0.80				
5			73.40	1.362	0.13431	7			25.81	3.874	0.58817	12	0		90.86	1.101	0.04163	128			15.14	6.604	0.81				
6			72.62	1.377	0.13894	8			25.54	3.916	0.59280	7	0		90.19	1.109	0.04483	130			14.70	6.802	0.83				
7			71.85	1.392	0.14357	9			25.27	3.958	0.59743	12	0		89.53	1.117	0.04804	132			14.27	7.006	0.84				
8			71.09	1.407	0.14820	10			25.00	4.000	0.60206	8	0		88.87	1.125	0.05124	134			13.86	7.215	0.85				
9			70.33	1.422	0.15283	11			24.73	4.043	0.60669	12	0		88.22	1.134	0.05444	136			13.46	7.431	0.87				
10			69.59	1.437	0.15746	12			24.47	4.086	0.61132	9	0		87.57	1.142	0.05764	138			13.07	7.654	0.88				
11			68.85	1.452	0.16209	13			24.21	4.130	0.61596	12	0		86.93	1.150	0.06085	140			12.69	7.883	0.89				
12			68.12	1.468	0.16672	14			23.96	4.174	0.62059	10	0		86.29	1.159	0.06405	142			11.78	8.486	0.92				
13			67.40	1.484	0.17136	15			23.70	4.219	0.62522	12	0		85.65	1.167	0.06725	144			10.95	9.136	0.96				
14			66.68	1.500	0.17599	16			23.45	4.264	0.62985	11	0		85.02	1.176	0.07045	146			10.17	9.835	0.99				
15			65.98	1.516	0.18062	17			23.20	4.310	0.63448	12	0		84.40	1.185	0.07366	148			9.45	10.587	1.02				
16			65.28	1.532	0.18525	18			22.96	4.356	0.63911	13	0		83.78	1.194	0.07686	150			8.77	11.398	1.05				
17			64.58	1.548	0.18988	19			22.71	4.403	0.64374	12	0		83.16	1.202	0.08006	152			8.15	12.270	1.08				
18			63.90	1.565	0.19451	20			22.47	4.450	0.64837	13	0		82.55	1.211	0.08326	154			7.57	13.209	1.12				
19			63.22	1.582	0.19914	21			22.23	4.498	0.65301	12	0		81.95	1.220	0.08647	156			7.03	14.220	1.15				
20			62.55	1.599	0.20377	22			22.00	4.546	0.65764	13	0		81.35	1.229	0.08967	158			6.53	15.308	1.18				
21			61.89	1.616	0.20841	23			21.76	4.595	0.66227	14	0		80.75	1.238	0.09287	160			6.07	16.479	1.21				
22			61.23	1.633	0.21304	6	0		21.53	4.644	0.66690	15	0		80.15	1.248	0.09607	162			5.64	17.740	1.24				
23			60.58	1.651	0.21767	1	0		21.30	4.694	0.67153	16	0		79.56	1.258	0.09927	164			5.24	19.098	1.28				
2	0		59.94	1.668	0.22230	2	0		21.08	4.744	0.67616	17	0		78.98	1.266	0.10248	166			4.86	20.599	1.31				
1	1		59.30	1.686	0.22693	3	0		20.85	4.795	0.68079	18	0		78.40	1.275	0.10568	168			4.52	22.133	1.34				
2	2		58.67	1.704	0.23156	4	0		20.63	4.846	0.68542	19	0		77.82	1.285	0.10888	170			4.20	23.626	1.37				
3	3		58.05	1.723	0.23619	5	0		20.41	4.898	0.69006	20	0		77.25	1.294	0.11208	172			3.90	25.160	1.40				
4	4		57.43	1.741	0.24082	6	0		20.20	4.951	0.69469	21	0		76.69	1.304	0.11529	174			3.62	26.713	1.44				
5	5		56.83	1.760	0.24546	7	0		19.98	5.004	0.69932	22	0		76.13	1.313	0.11849	176			3.36	28.292	1.47				
6	6		56.22	1.779	0.25009	8	0		19.77	5.058	0.70395	23	0		75.56	1.323	0.12169	178			3.12	30.000	1.50				
7	7		55.63	1.798	0.25472	9	0		19.56	5.112	0.70858	24	0		75.00	1.333	0.12489	180			2.90	31.749	1.53				
8	8		55.04	1.817	0.25935	10	0		19.35	5.167	0.71321	25	0		74.46	1.343	0.12810	182			2.70	33.536	1.56				
9	9		54.45	1.836	0.26398	11	0		19.15	5.222	0.71784	26	0		73.93	1.353	0.13130	184			2.50	35.362	1.60				
10	10		53.88	1.856	0.26861	12	0		18.95	5.278	0.72247	27	0		73.40	1.363	0.13450	186			2.33	37.233	1.63				
11	11		53.30	1.876	0.27324	13	0		18.75	5.335	0.72711	28	0		72.87	1.373	0.13770	188			2.16	39.149	1.66				
12	12		52.74	1.896	0.27787	14	0		18.55	5.392	0.73174	29	0		72.35	1.383	0.14091	190			2.01	41.109	1.69				
13	13		52.18	1.916	0.28251	15	0		18.35	5.450	0.73637	30	0		71.82	1.393	0.14411	192			1.86	43.210	1.72				
14	14		51.63	1.937	0.28714	16	0		18.16	5.508	0.74100	31	0		71.30	1.404	0.14731	194			1.73	45.456	1.76				
15	15		51.08	1.958	0.29177	17	0		17.96	5.567	0.74563	32	0		70.78	1.415	0.15051	196			1.61	47.844	1.79				
16	16		50.54	1.979	0.29640	18	0		17.77	5.627	0.75026	33	0		70.26	1.426	0.15371	198			1.49	50.372	1.82				
17	17		50.00	2.000	0.30103	19	0		17.58	5.687	0.75489	34	0		69.75	1.437	0.15691	200			1.39	52.944	1.85				
18	18		49.47	2.021	0.30566	20	0		17.40	5.748	0.75952	35	0		69.23	1.448	0.16011	202			1.29	55.660	1.88				
19	19		48.94	2.043	0.31029	21	0		17.21	5.810	0.76416	36	0		68.72	1.459	0.16331	204			1.20	58.424	1.91				
20	20		48.43	2.065	0.31492	22	0		17.03	5.872	0.76879	37	0		68.21	1.470	0.16651	206			1.13	61.236	1.94				
21	21		47.91	2.087	0.31956	23	0		16.85	5.935	0.77342	38	0		67.70	1.481	0.16971	208			1.06	64.092	1.97				
22	22		47.40	2.110	0.32419	7	0		16.67	5.999	0.77805	39	0		67.19	1.492	0.17291	210			0.96	66.992	2.00				
23	23		46.90	2.132	0.32882	8	0		16.49	6.063	0.78268	40	0		66.68	1.503	0.17611	212			0.89	69.932	2.03				
3	0		46.40	2.155	0.33345	12	0		16.31	6.127	0.78731	41	0		66.17	1.514	0.17931	214			0.83	72.912	2.06				
1	1		45.91	2.178	0.33808	18	0		16.13	6.191	0.79194	42	0		65.66	1.525	0.18251	216			0.77	75.932	2.09				
2	2		45.42	2.201	0.34271	8	0		15.95	6.255	0.79657	43	0		65.15	1.536	0.18571	218			0.72	78.992	2.12				
3	3		44.94	2.225	0.34734	6	0		15.77	6.319	0.80120	44	0		64.64	1.547	0.18891	220			0.66	82.092	2.15				
4	4		44.47	2.249	0.35197	12	0		15.60	6.383	0.80584	45	0		64.13	1.558	0.19211	222			0.62	85.232	2.18				
5	5		43.99	2.273	0.35661	18	0		15.42	6.447	0.81047	46	0		63.62	1.569	0.19531	224			0.57	88.412	2.21				
6	6		43.53	2.297	0.36124	6	0		15.25	6.511	0.81510	47	0		63.11	1.580	0.19851	226			0.53	91.632	2.24				
7	7		43.07	2.322	0.36587	12	0		15.08	6.575	0.81973	48	0		62.60	1.591	0.20171	228			0.49	94.892	2.27				
8	8		42.61	2.347	0.37050	18	0		14.91	6.639	0.82436	49	0		62.09	1.602	0.20491	230									
9	9		42.16	2.372	0.37513	6	0		14.74	6.703	0.82899	50	0		61.58	1.613	0.20811	232									
10	10		41.71	2.398	0.37976	12	0		14.57	6.767	0.83362	51	0		61.07	1.624	0.21131	234									
11	11		41.27	2.423	0.38439	18	0		14.40	6.831	0.83825	52	0		60.56	1.635	0.21451	236									
12	12		40.83	2.449	0.38902	6	0		14.23	6.895	0.84288	53	0		60.05	1.646	0.21771	238									
13	13		40.40	2.475	0.39366	12	0		14.06	6.959	0.84751	54	0		59.54	1.657	0.22091	240									
14	14		39.97	2.502	0.39829	18	0		13.89	7.023	0.85214	55	0		59.03	1.668	0.22411	242									
15	15		39.54	2.529	0.40292	6	0		13.72	7.087	0.85677	56	0		58.52	1.679	0.22731	244									
16	16		39.12	2.556	0.40755	12	0		13.55	7.151	0.86140	57	0		58.01	1.690	0.23051	246									
17	17		38.71	2.583	0.41218	18	0		13.38	7.215	0.86603																

Constituents of Living Matter

<i>Carbohydrates</i>	308	<i>Digestive enzymes</i>	405
Monosaccharides.....	308	Proteolytic enzymes (proteases, peptide hydrolases).....	405
Stereochemistry of sugars.....	308	Glycoside hydrolases (glycosidases).....	405
Amino sugars.....	311	Lipases and other ester hydrolases (esterases).....	405
Sugar phosphates.....	312	Nucleases.....	406
Polyhydric alcohols.....	312	<i>Synthesis of cell constituents from glucose</i>	420
Primary oxidation products of carbohydrates.....	312	The oxidative pentose phosphate cycle.....	420
Oligosaccharides.....	312	Glucuronic acid and iduronic acid.....	423
Polysaccharides.....	312	Formation of glucosamine and related amino sugars.....	423
<i>Amino acids</i>	329	Biosynthesis of L-fucose in mammalian tissues.....	423
Polypeptides.....	329	Formation and utilization of hexosamines and N-acetylneuraminic acid in mammals.....	424
<i>Nucleotides and nucleotides</i>	336	Extension of carbon chains by carbon dioxide fixation.....	424
<i>Nucleic acids</i>	351	Fatty acid synthesis.....	424
Synthesis of deoxyribonucleic acid (DNA).....	351	Formation of lecithin and cephalin.....	425
Synthesis of ribonucleic acid (RNA).....	352	Formation of triglyceride.....	426
Synthesis of proteins.....	353	Biosynthesis of cholesterol.....	426
Minor constituents of nucleic acids.....	354	Biosynthesis and metabolism of steroid hormones of the adrenal cortex and gonads.....	428
<i>Porphyrins</i>	355	Biosynthesis and metabolism of oestrogens.....	430
Iron porphyrins (haem derivatives).....	359	Formation of serine and glycine.....	432
Bile pigments.....	362	Formation of glutamic acid.....	432
Chlorophylls.....	362	Formation of proline and hydroxyproline.....	432
Cyanocobalamin (vitamin B ₁₂).....	363	Formation of histidine.....	432
<i>Lipids</i>	365	<i>Synthesis of cell constituents from amino acids</i>	433
Fatty acids.....	373	Formation of purines.....	433
Prostaglandins.....	373	Transfer of groups containing one carbon atom.....	436
Acylglycerols (fats).....	374	Formation of porphyrins.....	437
Alkoxylglycerides.....	374	Formation of creatine.....	437
Glycoglycerides.....	375	Formation of glutathione.....	438
Phospholipids (phosphatides).....	375	Formation of bile acid conjugates.....	438
Sphingolipids.....	376	Formation of taurocholic acid.....	438
Waxes.....	377	Formation of pyrimidines.....	439
<i>Steroids</i>	378	Conversion of phenylalanine to tyrosine.....	440
<i>Enzymes</i>	382	Formation of noradrenaline and adrenaline.....	440
Nomenclature of enzymes.....	382	Formation of thyroid hormones.....	440
Specificity of enzymes.....	382	Formation of melanin.....	440
Structure of enzymes and mechanism of enzyme action.....	382	Formation and degradation of 5-hydroxytryptamine (serotonin).....	441
Enzyme kinetics.....	382	Synthesis of carbohydrate from amino acids and other non-carbohydrate precursors (gluconeogenesis).....	441
Classification and numbering of enzymes.....	385	<i>Detoxication mechanisms</i>	442
<i>Metabolism</i>		Synthesis of urea.....	442
<i>General aspects</i>	387	Acetylation of amines.....	444
Energy metabolism.....	387	Formation of glycine conjugates.....	444
Cell metabolism.....	388	Formation of esters of sulphuric acid.....	445
<i>Energy-supplying reactions</i>	389	Formation of phenylacetylglutamine.....	445
Intermediate stages of carbohydrate degradation.....	389	Formation of mercapturic acids.....	445
Oxidative degradation of fat.....	391	<i>Inborn Errors of Metabolism</i>	
Intermediate stages of the degradation of amino acids.....	391	Introduction.....	446
Degradation of individual amino acids.....	394	Haemoglobinopathies.....	446
Degradation of food constituents other than carbohydrate, fat and protein.....	399	Inborn errors of amino-acid metabolism.....	448
Degradation of the principal foodstuffs.....	401	Inborn errors of carbohydrate metabolism.....	450
Mechanism of biological oxidations.....	402	Inborn defects of renal transport mechanisms.....	452
The key position of adenosine triphosphate (ATP) in biological energy transformations.....	404	Inborn errors of purine and pyrimidine metabolism.....	453
		Hyperbilirubinaemia and porphyria.....	454
		Lipidoses.....	455
		Inborn errors of corticosteroid metabolism.....	456

(For references see page 312)

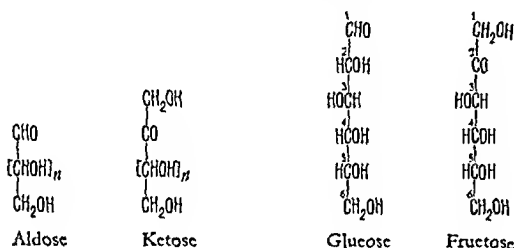
Carbohydrates[†]

Carbohydrates are carbon compounds containing hydrogen and oxygen in the ratio 2:1, their general empirical formula being $C_x(H_2O)_y$ **. The term is also extended, however, to oxidation and reduction products of carbohydrates proper, as well as to their simple derivatives such as amino and phosphorylated sugars.

Carbohydrates are frequently referred to as 'sugars' (saccharides) because many of them possess a sweet taste*** but actually the term 'sugar' is only loosely defined and may denote a wide variety of carbohydrate compounds. To the carbohydrate chemist, however, it means a mono- or oligosaccharide but *not* a polysaccharide (see below). Mono- and oligosaccharides are given names with the suffix '-ose', e.g., glucose, fructose, lactose.

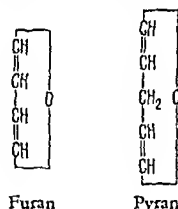
Monosaccharides

Carbohydrates that cannot be split further by hydrolysis are called simple sugars or monosaccharides. Their general empirical formula is $[C(H_2O)]_n$, and they are classed as aldehydic alcohols (aldoses) or ketonic alcohols (ketoses). Those of importance to mammals are listed in Table 1 (pages 313-316).

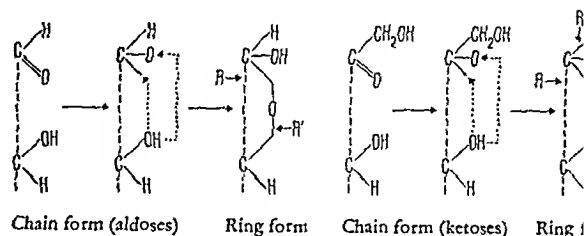


Sugars with chain lengths of 3, 4, 5, 6, etc. carbon atoms are known as trioses, tetroses, pentoses, hexoses, etc.†. The numbering convention is shown above in the structures of glucose and fructose.

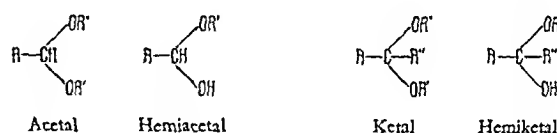
The open-chain form of sugars (aldehyde or ketone form) normally occurs only in aqueous solution, where it is a transitional form in equilibrium with the ring form. The latter is the rule with carbohydrates of longer chain length, and with few exceptions the ring is usually 5- or 6-membered. By analogy with the similar heterocyclic compounds†† furan and pyran, these ring forms are known as *furanoses* and *pyranoses* respectively:



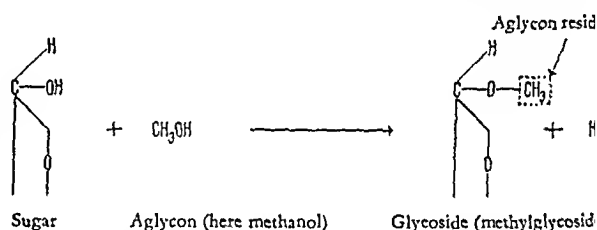
The ring forms are formed from chain forms by the reaction of the hydroxyl group in the 4 or 5 position with the carbonyl group. Carbon atom 4 is involved in the case of furanoses, carbon atom 5 in the case of pyranoses. This results in the formation of an oxygen bridge between the carbon atoms concerned and of a hydroxyl group on the carbon atom of the original carbonyl group:



The compound formed is an intramolecular hemiacetal (when derived from an aldose) or hemiketal (when derived from a ketose).



The hydroxyl group attached to the hemiacetal or hemiketal carbon atom (C-1 or C-2 respectively) is particularly reactive and known as the glycosidic hydroxyl. It combines readily with alcoholic or phenolic groups of other molecules, and when the reaction takes place with a compound that is not another sugar (an aglycon), the resulting compound is known as a *glycoside*:



When the reaction takes place with a molecule of another sugar the resulting compound is known not as a glycoside but as a disaccharide (cf. 'Oligo- and Polysaccharides', page 312).

Stereochemistry of sugars

The stereoisomerism of sugars and related substances is of particular importance in biochemistry*, and for this reason it will be dealt with in some detail here. For a more thorough treatment of the subject see HONEYMAN². A carbon atom with four different substituents, for example C-2 of glyceraldehyde, is known as an *asymmetric* carbon atom. This grouping cannot be superimposed on its mirror image and the resulting lack of symmetry gives rise to a type of isomerism associated with optical activity. The two possible spatial configurations of the substituents can be readily seen if one imagines the asymmetric C atom to be in the middle of a regular tetrahedron with the valencies pointing to the corners. The two possible configurations of glyceraldehyde shown as an example in Figure 1 cannot in any way be superimposed one upon the other. They are related to one another as an object to its mirror image, and are known as enantiomorphs. No such asymmetry exists with a carbon atom possessing at least two identical substituents.

Enantiomorphous isomers are optically active, i.e., in solution one of the isomers rotates the plane of polarized light to the right, the other an equal amount to the left. The degree of rotation depends on the length of the polarimeter tube, on the wave length of the polarized light, on the concentration, and on the solvent and its temperature**. The direction of the rotation was originally indicated by prefixing the name of the isomer by *dextro* (*d*-) and *laevo* (*l*-)

* Stereoisomerism is of importance in nature not only for carbohydrates but for all compounds where stereoisomers are possible. This is because as a rule only specific stereoisomers are synthesized or degraded in naturally occurring reactions (this is a characteristic difference compared to laboratory synthesis). One reason is the stereospecificity of many enzymes, but the fundamental mechanism is unknown.

** The specific rotation $[\alpha]$ is defined as the rotation in degrees of 1g of substance in 1ml of solution in a tube with a length of 10 cm. The D-line of sodium is as a rule used as a source of light. The temperature, wave length of the incident light, nature of the solvent and the concentration must also be included where these diverge from the definition, e.g., $[\alpha]_D^{20}$, 20% (H₂O) = +12°.

* This chapter, 'Constituents of Living Matter', has been written in consultation with J. R. QUAYLE (Department of Microbiology, University of British Columbia), J. M. LOWENSTEIN (Graduate Department of Biochemistry, Brandeis University, Waltham, Mass., USA) and P. R. RAGGATT (Department of Biochemistry, University of Oxford, England).

** There are compounds with this empirical formula that do not fall into the category of carbohydrates, such as acetic acid, lactic acid, phloroglucinol.

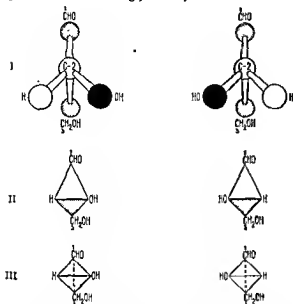
*** The sweetest of the sugars is fructose. Polysaccharides have no taste. † According to BEILSTEIN (1938) these names are derived from the number of oxygen atoms. In the case of 'ordinary' monosaccharides $[C(H_2O)]_n$ both nomenclatures are identical. They are different in the case of substituted and deoxy sugars. In general the nomenclature based on the number of carbon atoms is the more commonly used and permits a better understanding of carbohydrate metabolism (anabolism of the carbon chain from small molecules and its subsequent catabolism).

†† Heterocycles are ring molecules in which apart from carbon atoms the ring contains at least one atom of another element.

Constituents of Living Matter - Carbohydrates

(For references see page 312)

Fig 1 Stereoisomerism of glyceraldehyde



I Atomic models

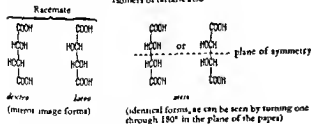
II Tetrahedral representation of I. The edge of the tetrahedron joining C-1 and C-3 (imagined to be in or below the plane of the paper) is invisible, as is also the asymmetric carbon atom C-2 lying inside the tetrahedron.

III Conventional representation of the tetrahedron. The edge between C-1 and C-3 in the plane of the paper is indicated by a broken line; the other edges (all above the plane of the paper) by full lines.

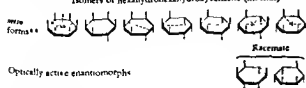
respectively. The alternative symbols (+) and (-) are now more commonly used*.

A racemate must not be confused with an optically inactive *meso* form. A *meso* form may arise in the case of a molecule possessing more than one asymmetric centre where the configuration is such that there is a plane or centre of symmetry in the molecule as a whole. The various directions of rotation then cancel each other out within the molecule (internal compensation). These racemic and *meso* forms are illustrated by the cases of tartaric acid and hexahydrohexahydroxybenzene.

Isomers of tartaric acid



Isomers of hexahydrohexahydroxybenzene (inositol)



(The vertical lines indicate the positions of the OH groups, the broken lines the planes of symmetry.)

* The use of the letters *d* and *l* to denote optical rotation is now discouraged in favour of *d* and *l*, or better (+) and (-), which is likewise preferred for racemates.

** Although all structures are *meso* forms and optically inactive, the name *meso*inositol is confined to the fifth compound from the left.

Meso forms do not occur in the case of sugars since the carbonyl group on one side of the ring renders *meso*-symmetry impossible.

The classification of carbohydrate molecules is based on its relationship to the simplest optically active sugar, glyceraldehyde, to which ROSANOFF² arbitrarily assigned the following configurations:

Projection formulae (Fischer)



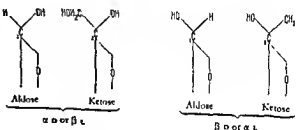
(With the carbonyl group at the top, the hydroxyl group is written on right of the asymmetric carbon atom in the case of the dextro compound, and on the left in the case of the lacto compound.)

the parent substance can increase or decrease or even be reversed.

methods

With a few exceptions, all naturally occurring sugars belong

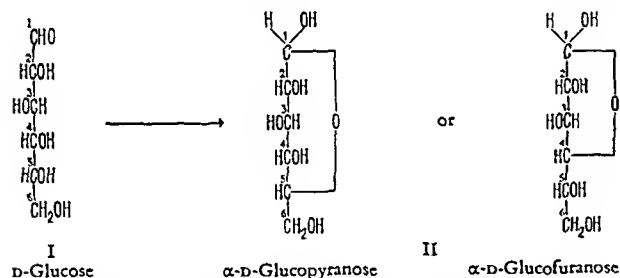
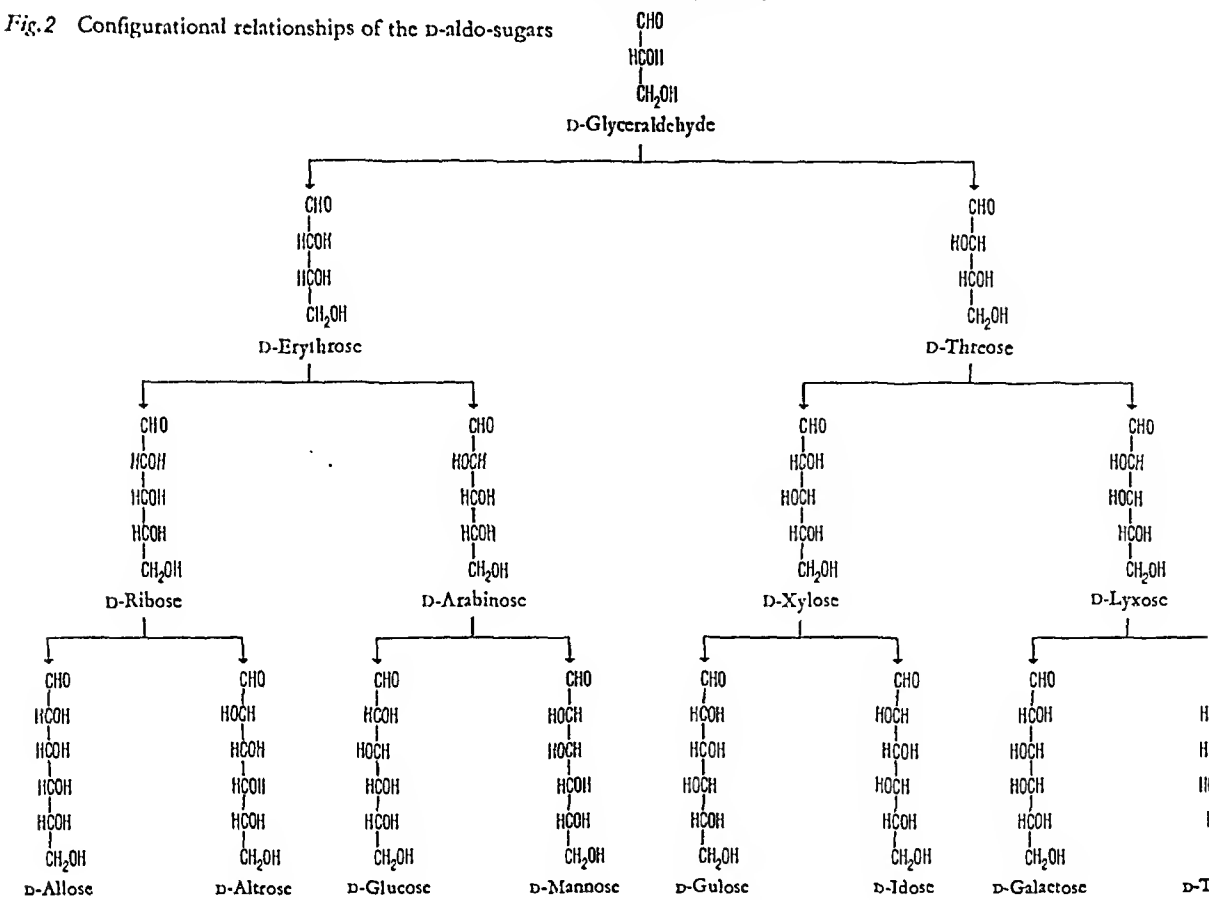
group, thus introducing an additional asymmetric centre. The stereoisomers of a cyclic sugar molecule arising in this way are denoted by the symbols α and β (after HUGGINS³), the designation being given to the isomer in the D-series that is more strongly dextro-rotatory and to the isomer in the L-series that is more



The α - and β -anomers...

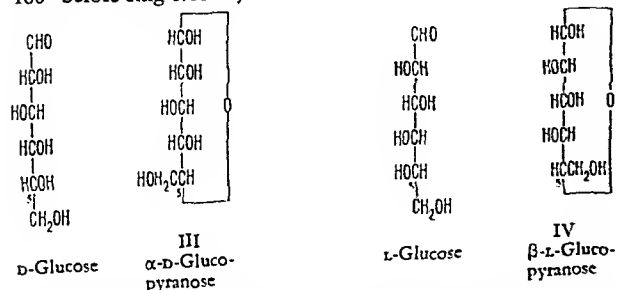
(For references see page 312)

Fig. 2 Configurational relationships of the D-aldo-sugars



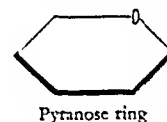
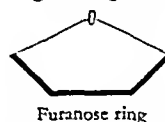
The ring formulae of type II are commonly used because their relationship to the chain formula I can readily be seen. However, although the steric relations of the secondary alcohol groups (-CHOH) forming the ring are correctly represented by these formulae, they do not give a true picture of the steric configuration around the C atom to which the oxygen bridge is attached (C-5 in the case of glucopyranose, C-4 in the case of glucofuranose). This arises from the fact that it is the convention, as described above, to write this group in the chain formulae of the D-series with the OH group on the right.

In the case of the pyranoses, a more correct type of projection formula is that illustrated by III and IV for glucose (derived by imagining the bond between C-4 and C-5 to be rotated through 180° before ring closure):

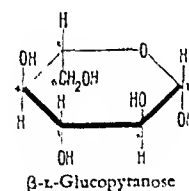
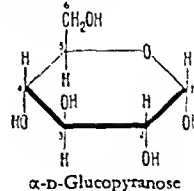


In formulae III and IV, however, the D- and L-configurations respectively of the OH group attached to C-5 are no longer readily

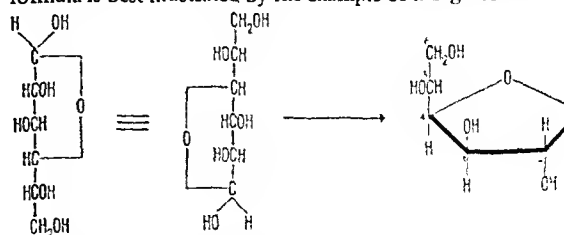
recognizable. These defects of the FISCHER projection for led HAWORTH to introduce a type of ring formula in which steric relations of the groups are shown unequivocally. This is imagined as being looked at obliquely from above, the thickened edges being those nearest to the observer:



The positions of the substituents correspond to those in formulae of type III and IV:



In the case of the furanose forms of hexoses, ring closure results in the formation of a side chain. When, as in the case of glucofuranose, this side chain contains an asymmetric carbon atom, its configuration in the HAWORTH formula must be shown by means of an appropriate convention. The derivation from the projection formula is best illustrated by the example of $\alpha\text{-D-glucofuranose}$:

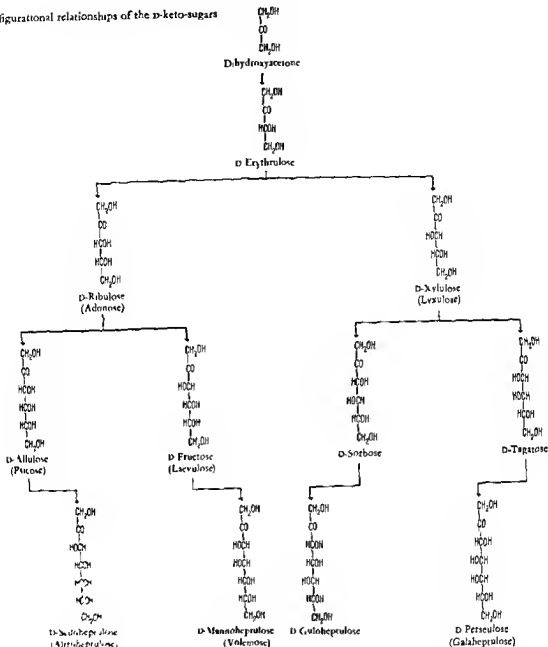


For convenience in writing the formulae of polysaccharides and other complex sugar compounds, the HAWORTH rings are sometimes

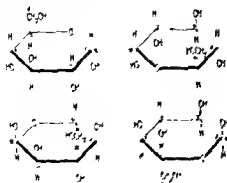
Constituents of Living Matter - Carbohydrates

(For references see page 312)

Configurational relationships of the D-keto-sugars



native positions for α-D-glucopyranose are as follows



It is now known that the pyranose ring is not planar, of its properties can be explained on the assumption that 'chair' form. The furanose ring is usually planar. For further of the conformational analysis see the literature⁶

Amino sugars⁷

Amino sugars are components of polysaccharides (see literature⁸)

of antibiotics⁹

The glucose units which are present in antibiotics are of the chair form. The furanose ring is usually planar. For further of the conformational analysis see the literature⁶

Sugar phosphates¹⁰

Phosphorylated sugars are intermediates in glycolysis; they are components of nucleic acids, nucleotides and polysaccharides¹¹ (see Table 2, pages 317–321).

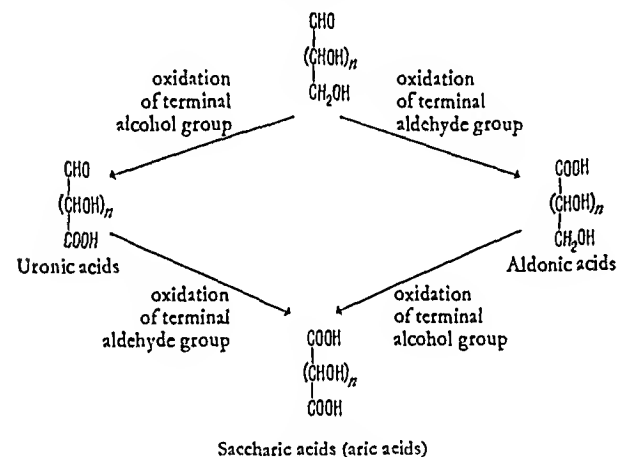
The stability of phosphate groups toward acid or alkaline hydrolysis varies over a wide range¹² and, as yet, detailed correlation between the rates of hydrolysis and the position of the groups has not been made. Under conditions of acid or alkaline hydrolysis, migration of the phosphate group may occur, e.g., in the case of the phosphoglyceric acids¹³.

Polyhydric alcohols¹⁴

These compounds, which may be considered as reduction products of the monosaccharides, are of wide occurrence in plants but of limited occurrence in mammalian tissue. They are mostly crystalline compounds, generally possessing a sweet taste and devoid of any reducing properties. Those of importance to mammals are listed in Table 3 (page 322).

Primary oxidation products of carbohydrates

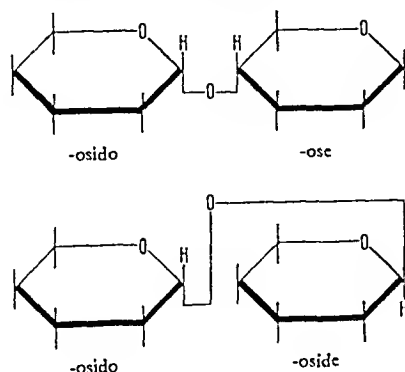
The nomenclature of the products of the oxidation of the terminal groups of aldoses is derived as follows:



Oxidation products of carbohydrates of importance to mammals are listed in Table 4 (page 323).

Oligosaccharides

Oligosaccharides are composed of monosaccharide molecules or their derivatives linked together through glycosidic linkages. The linkages may be glycosidic on one side only or on both sides. In the nomenclature of oligosaccharides, the sugar units in compounds of the former type are given the suffixes '-osido' and '-ose', while those in the latter type are indicated by '-osido' and '-oside'. This is illustrated by the following scheme:



The term oligosaccharide is generally used to designate compounds containing between two and ten monosaccharide units per molecule. Oligosaccharides may be reducing or nonreducing, depending on the presence or absence of free hemiacetal hydroxyl groups. The constituent monosaccharides are set free from an oligosaccharide by acid or enzymic hydrolysis.

The principal oligosaccharides of importance to mammals are given in Table 5 (page 324). A great variety of oligosaccharides encountered in the plant kingdom.

Polysaccharides¹⁵

Polysaccharides, like oligosaccharides, are built up from a variety of monosaccharide units and their derivatives. They differ from oligosaccharides in that their molecules contain from ten to several thousand monosaccharide units. The most common recurring constituent is D-glucose. However, D-mannose, D- and L- galactose, D-xylose, L-arabinose, uronic acids (D-glucuronic, D-galacturonic and D-mannuronic acids), amino sugars (D-glucosamine, D-galactosamine, their N-acetyl derivatives and sulphate esters) are also found. In contrast with the oligosaccharides many of the polysaccharides are insoluble and nonreducing.

Their structure has been investigated by chemical methods¹, e.g., by methylation and subsequent hydrolysis, by periodate oxidation, and by enzymic methods¹⁶. The determination of the molecular size of polysaccharides involves physical measurement of properties such as osmotic pressure, behaviour on ultracentrifuging, viscosity and light scattering¹⁷.

Polysaccharides may serve as:

- (a) structural materials, e.g., cellulose (plants), chitin (insects and crustaceae), chondroitin sulphate (cartilage)¹⁸,
- (b) food storage, e.g., glycogen (animals), starch (plants),
- (c) lubricants in synovial fluids, constituents of special tissues (vitrous body of the eye; connective tissue), components of mucopolysaccharides, heparin, blood-group substances¹⁹.

The principal polysaccharides of importance to mammals are listed in Table 6 (pages 325–328).

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- ¹ For reviews see GILMAN et al. (Eds.), *Organic Chemistry: An Advanced Treatise*, vol. 2, 2nd ed., Wiley, New York, 1943, page 1532; PERCIVAL E.G.V., *Structural Carbohydrate Chemistry*, Prentice-Hall, New York, 1950; PIGMAN, W. (Ed.), *The Carbohydrates*, Academic Press, New York, 1957.
- ² HONEYMAN, J., *An Introduction to the Chemistry of Carbohydrates*, Oxford University Press, Oxford, 1948.
- ³ ROSANOFF, M.A., *J. Amer. chem. Soc.*, **28**, 114 (1906).
- ⁴ BIJVOET, J.M., *Endavour*, **14**, 71 (1955).
- ⁵ HUDSON, C.S., *Advanc. Carbohydr. Chem.*, **3**, 1 (1948).
- ⁶ MILLS, J.A., *Advanc. Carbohydr. Chem.*, **10**, 1 (1955); CAPON and OVEREND *Advanc. Carbohydr. Chem.*, **15**, 11 (1960).
- ⁷ SALTON, M.R.J., *Ann. Rev. Biochem.*, **34**, 143 (1965); JEANLOZ and BALAZS, *The Amino Sugars*, vol. 2A, Academic Press, New York, 1965.
- ⁸ DUTCHER, J.D., *Advanc. Carbohydr. Chem.*, **18**, 259 (1963).
- ⁹ GOTTSCHALK, A., *The Chemistry and Biology of Sialic Acids and Related Substances*, Cambridge University Press, Cambridge, 1960.
- ¹⁰ For reviews see LELOIR, L.F., in ZECHMEISTER, L. (Ed.), *Progress in the Chemistry of Organic Natural Products*, vol. 8, Springer, Vienna, 1951, page 47; FOSTER and OVEREND, *Quart. Rev. chem. Soc. Lond.*, **11**, 61 (1957).
- ¹¹ For a general account see AVISON and HAWKINS, *Quart. Rev. chem. Soc. Lond.*, **5**, 171 (1951).
- ¹² See LELOIR, L.F., in ZECHMEISTER, L. (Ed.), *Progress in the Chemistry of Organic Natural Products*, vol. 8, Springer, Vienna, 1951, page 47.
- ¹³ See BALLOU and FISCHER, *J. Amer. chem. Soc.*, **76**, 3188 (1954).
- ¹⁴ For a review see LOHMAN, R.L., in PIGMAN, W. (Ed.), *The Carbohydrates*, Academic Press, New York, 1957, page 241; TOUSTER and SHAW, *Phytochem. Rev.*, **42**, 181 (1962).
- ¹⁵ For reviews see STACEY and BARKER, *Polysaccharides of Micro-Organisms*, Oxford University Press, Oxford, 1960; STACEY and BARKER, *Carbohydrates of Living Tissues*, Van Nostrand, London, 1962; MANNERS, D.J., *Advanc. Carbohydr. Chem.*, **12**, 261 (1957); BOUVENG and LINDBERG, *Advanc. Carbohydr. Chem.*, **15**, 53 (1960); ASPINALL, G.O., *Adv. Rev. Biochem.*, **31**, 79 (1962).
- ¹⁶ MANNERS, D.J., *Quart. Rev. chem. Soc. Lond.*, **9**, 73 (1955); MANNERS, D.J., *Advanc. Carbohydr. Chem.*, **17**, 371 (1962).
- ¹⁷ GREENWOOD, C.T., *Advanc. Carbohydr. Chem.*, **7**, 289 (1952).
- ¹⁸ Cf. KENT and WHITEHOUSE, *Biochemistry of the Amino Sugars*, Butterworth, London, 1957; HANG, G., in ZECHMEISTER, L. (Ed.), *Progress in the Chemistry of Organic Natural Products*, vol. 20,

Constituents of Living Matter – Carbohydrates

1/2 Monosaccharides of importance to mammals

Some of the more important sugars that are constituents of substances of medical interest are also included in this table

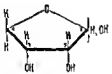
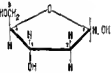
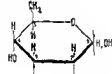

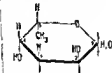
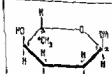
Name	Formula and mol wt.	Structure	Specific rotation	Occurrence
<i>Tetroses</i>				
Glyceraldehyde (2,3-dihydroxy-propanal)	$C_3H_6O_3$ 90.08	$\begin{array}{c} \text{CHO} \\ \\ \text{HOCH} \\ \\ \text{CH}_2\text{OH} \end{array}$	$[\alpha]_D^{20} + 13.5^\circ$	As phosphate ester (see Table 2, page 317)
Dihydroxyacetone (1,3-dihydroxy-propan-2-one)	$C_3H_6O_3$ 90.08	$\begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{CO} \\ \\ \text{CH}_2\text{OH} \end{array} \quad \text{or} \quad \begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{C(OH)} \\ \\ \text{CH}_2\text{OH} \end{array}$	Inactive	As phosphate ester (see Table 2, page 317)
<i>Tetroses</i>				
D-Erythrose	$C_4H_8O_4$ 120.11		$[\alpha]_D^{20} - 14.6^\circ$	As phosphate ester (see Table 2, page 317)
L-Erythrulose	$C_4H_8O_4$ 120.11	$\begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{CO} \\ \\ \text{HOCH} \\ \\ \text{CH}_2\text{OH} \end{array}$	$[\alpha]_D^{20} + 12^\circ$	As metabolically active phosphate ester (see Table 2, page 317)
2-Deoxy-D-ribose (2-deoxy-D-erythrulose, thymine, deoxyarabinose)	$C_5H_{10}O_4$ 134.13		$[\alpha]_D^{20} - 50^\circ$	Universal occurrence as constituent of nucleosides, nucleotides and nucleic acids. For phosphates see Table 3, page 318
D-Digitoxose (2-deoxy-D-erythrulose)	$C_5H_{10}O_4$ 148.16		$[\alpha]_D^{20} + 46.5^\circ$	Component of digitalis glycosides
<i>Pentoses</i>				
β-D-Arabinose	$C_5H_{10}O_5$ 150.13		$[\alpha]_D^{20} \sim 105^\circ$	In glycosides of aloe and berberis
L-Fucose (6-deoxy-L-galactose)	$C_6H_{12}O_5$ 164.16		$[\alpha]_D^{20} - 153^\circ \rightarrow +76^\circ$	Component of polysaccharides of human milk, b group substances, mucin, gum tragacanth (Table 5, page 324)
L-Rhamnose (6-deoxy-L-mannose, mulonicol)	$C_6H_{12}O_5$ 164.16		α -form, $1H_2O$ $[\alpha]_D^{20} - 9^\circ$ β -form, $[\alpha]_D^{20} + 38^\circ$	As glycoside in plant gums and mucins. Common component of mucic glycosides

Table 1 (continued) Monosaccharides of importance to mammals

Name*	Formula and mol. wt.	Structure	Specific rotation	Occurrence
D-Ribose (Rib) (D-ribofuranose)	$C_5H_{10}O_5$ 150.13		$[\alpha]_D^{20} - 23.7^\circ$ (4% soln.)	Universal occurrence as constituent of nucleosides, nucleotides and nucleic acids. For phosphates see Table 2, pages 317–318
D-Ribulose (D-erythrepentulose, D-adonose, D-arabulose)	$C_5H_{10}O_5$ 150.13	$\begin{array}{c} CH_2OH \\ \\ CO \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OH \end{array}$	—	As phosphate esters (see Table 2, page 318). Intermediary metabolite in glucose oxidation
D-Xylulose (D-threopentulose, D-xyloketose, D-lyxulose, D-lyxoketose)	$C_5H_{10}O_5$ 150.13	$\begin{array}{c} CH_2OH \\ \\ CO \\ \\ HOCH \\ \\ HCOH \\ \\ CH_2OH \end{array}$	$[\alpha]_D^{20} - 33^\circ$	As phosphate ester (see Table 2, page 318)
L-Xylulose (L-threopentulose, L-xyloketose, L-lyxulose, L-lyxoketose)	$C_5H_{10}O_5$ 150.13	$\begin{array}{c} CH_2OH \\ \\ CO \\ \\ HCOH \\ \\ HOCH \\ \\ CH_2OH \end{array}$	$[\alpha]_D^{20} + 33^\circ$	In urine in pentosuria
<i>Hexoses</i>				
D-Fructose (Fru) (2-keto-D-arabohexose, laevulose, fruit sugar)	$C_6H_{12}O_6$ 180.16		β -form: $[\alpha]_D^{20} - 133.5^\circ \rightarrow -92^\circ$	As phosphate esters (see Table 2, pages 318–319). Component of many polysaccharides (combined with glucose in sucrose). Has pyranose form when crystalline but furanose form in all natural products. Sweetest of all known sugars
D-Galactose (Gal) (cerebrose, brain sugar)	$C_6H_{12}O_6$ 180.16		α -form: $[\alpha]_D^{20} + 144^\circ \rightarrow +80.5^\circ$ β -form: $[\alpha]_D^{20} + 54^\circ \rightarrow +80.5^\circ$	Present in mammalian tissues as phosphate ester (see Table 2, page 319). Component of cerebroside and gangliosides, and of polysaccharides both as sugar and derived amino sugar (e.g., lactose, raffinose, stachyose)
D-Galactosamine (GalN) (D-chondrosamine, 2-amino-2-deoxy- D-galactose)	$C_6H_{12}NO_6$ 179.17		α -form, 1 HCl: $[\alpha]_D^{20} + 135^\circ \rightarrow +93^\circ$ β -form, 1 HCl: $[\alpha]_D^{20} + 39^\circ \rightarrow +93^\circ$	Widely distributed in nature as component of hyaluronic acid, mucopolysaccharides, cartilage, tendons (chondroitin), β -heparin, lipoids, cerebral gangliosides, blood-group substances, glycoproteins (see Table 6, pages 326–328)

* The three-letter symbols are those recommended by the Combined Commission on Biochemical Nomenclature of the International Union of Pure

and Applied Chemistry and the International Union of Biochemistry (*J. Biol. Chem.*, 241, 527 [1966]).

Table 1 (continued) Monosaccharides of importance to mammals

Name*	Formula and mol wt.	Structure	Specific rotation	Occurrence
N-Acetyl-D-galactosamine	$C_6H_{11}NO_5$ 221.21		$[\alpha]_D^{25} + 115^\circ \rightarrow + 80^\circ$	Form in which D-galactosamine (page 314) occurs as component of hyaluronic acid, etc.
D-Glucose (Glc, G) (dextrose, blood sugar, grape sugar, corn sugar)	$C_6H_{12}O_6$ 180.16		α -form $[\alpha]_D^{25} + 113.4^\circ \rightarrow + 52.5^\circ$ β -form $[\alpha]_D^{25} + 19.3^\circ \rightarrow + 52.5^\circ$	As phosphate esters (see Table 2, page 319). Most widely distributed of all sugars. Found free in many biological fluids, e.g., blood, lymph, cerebrospinal fluid. Component of polysaccharides both as sugar and amino sugar (see 'D-Glucosamine', below).
D-Glucosamine (GlcN) (chitosamine, 2-amino-2-deoxy- D-glucose)	$C_6H_{13}NO_5$ 179.17		α -form $[\alpha]_D^{25} + 100^\circ$ β -form $[\alpha]_D^{25} + 14^\circ \rightarrow$	
N-Acetyl-D-glucosamine	$C_{11}H_{19}NO_6$ 221.21		-	Form in which D-glucosamine occurs as component of chitin, etc.
3-O-Carboxyglucosamine (muramic acid)	$C_{11}H_{17}NO_8$ 251.24		$[\alpha]_D^{25} + 109^\circ$ (water)	Component of bacterial cell walls ¹
N-Methyl-L-glucosamine	$C_7H_{15}NO_5$ 193.20		-	Component of streptomycin
D-Mannose (Man) (semulose)	$C_6H_{12}O_6$ 180.16		α form $[\alpha]_D^{25} + 29.9^\circ \rightarrow + 14.5^\circ$ β -form $[\alpha]_D^{25} - 16.3^\circ \rightarrow + 14.5^\circ$	As phosphate ester (see Table 2, page 320). Widely distributed as component of mannans and hemicelluloses. Limited occurrence as component of glycoproteins.

* See footnote, page 314

¹ Kaczka H J, *Biochem Soc Symp*, No 22, 55 (1963)

Table 1 (concluded) Monosaccharides of importance to mammals

Name	Formula and mol. wt.	Structure	Specific rotation	Occurrence
<i>N</i> -Acetyl- <i>D</i> -mannosamine	$C_8H_{15}NO_4$ 221.21		$[\alpha]_D^{20} - 9.4^\circ \rightarrow + 9.7^\circ$	Intermediate in biosynthesis of <i>N</i> -acetylneuraminic acid
<i>Heptose</i>				
<i>D</i> -Sedoheptulose (<i>D</i> -alloketoheptose, <i>D</i> -alloheptulose)	$C_7H_{14}O_7$ 210.19		$[\alpha]_D^{20} + 2-3^\circ$ Ba salt: $[\alpha]_{440}^{20} + 8^\circ$	As phosphate esters (see Table 2, page 321)
<i>Nonoses</i>				
<i>N</i> -Acetylneuraminic acid	$C_{11}H_{19}NO_8$ 309.28		$[\alpha]_D^{25} - 32^\circ$ No mutarotation	Component of mucins of epithelial secretions (e.g., digestive and urinary tracts), serglycoproteins, milk oligosaccharides, brain gangliosides, erythrocyte stroma, bacterial cell walls
<i>N</i> -Glycolylneuraminic acid	$C_{11}H_{17}NO_{10}$ 325.27		$[\alpha]_D^{25} - 32^\circ$	Component of mucins of epithelial secretions, serglycoproteins, erythrocyte stroma. Often in the same molecule as <i>N</i> -acetylneuraminic acid
5- <i>N</i> ,4- <i>O</i> -Diacetylneuraminic acid	$C_{13}H_{21}NO_{10}$ 351.31		$[\alpha]_D^{25} - 61^\circ$ No mutarotation	Equine submaxillary mucin
5- <i>N</i> ,7- <i>O</i> -Diacetylneuraminic acid	$C_{13}H_{21}NO_{10}$ 351.31		$[\alpha]_D^{25} + 8^\circ$ After 400 h $- 17^\circ$	Bovine submaxillary mucin
5- <i>N</i> -Acetyl, <i>O</i> -diacetylneuraminic acid	$C_{15}H_{23}NO_{11}$ 393.35		$[\alpha]_D^{25} + 9^\circ$	Bovine submaxillary mucin

Sugar phosphates of importance to mammals

(Not including nucleotides, for which see Tables 10c, 11 and 12, pages 342-350)












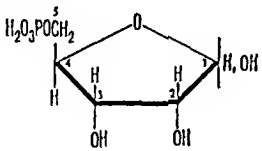
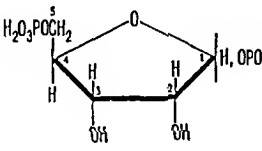
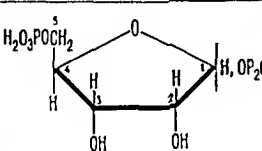
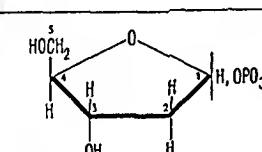
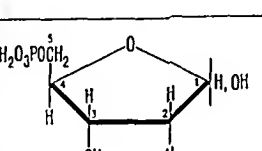
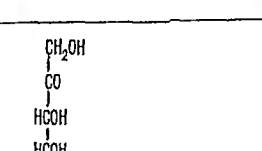
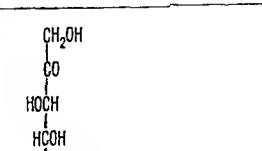
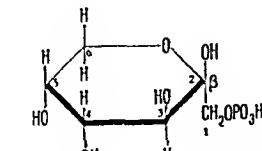
Name	Formula and mol. wt.	Structure	Elementary composition			Specific rotation	Biological function	Reference (see page 321)
			C	H	P			
Isoxyacetone phosphate	$C_3H_5O_5P$ 170.06		21.19	4.15	18.21	—	Intermediate of glycolysis	1
Dihydroxyacetone phosphate (BAYER 10')	$C_3H_5O_5P$ 170.06		21.19	4.15	18.21	$[\alpha]_D^{25} + 14^\circ$	Intermediate of glycolysis	2
Glycerol phosphate	$C_3H_7O_5P$ 172.08		20.94	5.27	18.00	$[\alpha]_D^{25} - 1.45^\circ$ (Ba salt)	Intermediate of fat metabolism Component of phospholipids	3
Pyruvic acid phosphate (FESSLING ester')	$C_3H_5O_5P$ 186.06		19.37	3.79	16.65	$[\alpha]_D^{25} + 13^\circ$ (1-N HCl) $[\alpha]_D^{25} + 3.6^\circ$ (water)	Intermediate of glycolysis	4
Pyruvic acid phosphate	$C_3H_5O_5P$ 186.06		19.37	3.79	16.65	$[\alpha]_D^{25} - 14.5^\circ$ (1-N HCl)	Intermediate of glycolysis	5
Pyruvic acid 1-diphosphate	$C_3H_5O_7P_2$ 266.04		13.54	3.03	23.29	$[\alpha]_D^{25} - 2.3^\circ$	Intermediate of glycolysis	6
Pyruvic acid 3-diphosphate	$C_3H_5O_7P_2$ 266.04		13.54	3.03	23.29	$[\alpha]_D^{25} - 2.3^\circ$	Intermediate of glycolysis	7
Pyruvic acid enol phosphate (pyruvic acid)	$C_3H_5O_5P$ 168.04		21.44	3.00	18.43	—	Intermediate of glycolysis	8
Erythrose phosphate	$C_4H_7O_5P$ 200.09		24.01	4.53	15.48	—	Intermediate of pentose phosphate cycle	9
Erythrulose phosphate	$C_4H_7O_5P$ 200.09		24.01	4.53	15.48	—	Function not known	10
-Ribose-phosphate (uranose form)	$C_5H_{11}O_5P$ 230.11		26.10	4.82	13.46	—	Intermediate of nucleotide metabolism	11

Table 2 (continued) Sugar phosphates of importance to mammals

Name	Formula and mol. wt.	Structure	Elementary composition			Specific rotation	Biological function	
			C	H	P			
D-Ribose 5-phosphate (furanose form)	$C_5H_{11}O_8P$ 230.11		26.10	4.82	13.46	$[\alpha]_D^{20} + 16.5^\circ$	Intermediate of pentose phosphate cycle and nucleotide synthesis	1
D-Ribose 1,5-diphosphate (furanose form)	$C_5H_{11}O_{11}P_2$ 310.09		19.37	3.90	19.98	—	Intermediate of interconversion of ribose 1-phosphate and ribose 5-phosphate	1
D-Ribose 5-phosphate-1-pyrophosphate (5-phosphorihosyl-1-pyrophosphate)	$C_8H_{13}O_{14}P_3$ 390.07		15.40	3.36	23.82	—	Intermediate of nucleotide synthesis	1
Deoxyribose 1-phosphate (furanose form)	$C_5H_{11}O_7P$ 214.11		28.05	5.18	14.47	—	Product of nucleoside degradation	12
Deoxyribose 5-phosphate (furanose form)	$C_5H_{11}O_7P$ 214.11		28.05	5.18	14.47	—	Component of deoxynucleic acids and deoxy-nucleotides	16
D-Ribulose 5-phosphate	$C_5H_{11}O_8P$ 230.11		26.10	4.82	13.46	$[\alpha]_D^{20} - 40^\circ$	Intermediate of pentose phosphate cycle	17
D-Xylulose 5-phosphate	$C_5H_{11}O_8P$ 230.11		26.10	4.82	13.46	—	Intermediate of pentose phosphate cycle	18
D-Fructose 1-phosphate (pyranose form) ('ROBISON-TANKO ester')	$C_6H_{13}O_8P$ 260.14		27.70	5.04	11.91	$[\alpha]_D^{20} - 30.4^\circ$	Intermediate of glycolysis	19

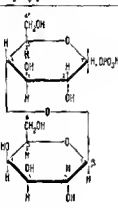
2 (continued) Sugar phosphates of importance to mammals

Name	Formula and mol wt.	Structure	Elementary composition			Specific rotation	Biological function	Reference (see page 321)
			C	H	P			
Uctose phosphate (ranose form) (NEUBERG ester)	$C_6H_{11}O_6P$ 260.14		27.70	5.04	11.91	$[\alpha]_D^{25} + 3.58^\circ$ (Ba salt)	Intermediate of glycolysis	20
Uctose 6-diphosphate (ranose form) (HARDEN-YOUNG ester)	$C_6H_{11}O_8P_2$ 340.12		21.19	4.15	18.21	$[\alpha]_D^{25} + 4.1^\circ$	Intermediate of glycolysis	21
-Galactose phosphate (yanose form)	$C_6H_{11}O_6P$ 260.14		27.70	5.04	11.91	$[\alpha]_D^{25} + 148.5^\circ$	Intermediate of galactose metabolism	22
Galactosamine phosphate	$C_6H_{11}NO_6P$ 259.15		27.81	5.45	11.95	-	Formed from galactosamine in brain tissue extracts and <i>Saccharomyces fragilis</i>	23
D-Glucose 1-phosphate (pyranose form) (CORI ester)	$C_6H_{11}O_6P$ 260.14		27.70	5.04	11.91	$[\alpha]_D^{25} + 120^\circ$	Intermediate of glucose-glycogen interconversion	24
Glucose 6-phosphate (pyranose form) (ROBINSON ester)	$C_6H_{11}O_6P$ 260.14		27.70	5.04	11.91	$[\alpha]_D^{25} + 34.2^\circ$	Intermediate of glycolysis	25
D-Glucose 1,6-diphosphate (pyranose form)	$C_6H_{11}O_8P_2$ 340.12		21.19	4.15	18.21	$[\alpha]_D^{25} - 19^\circ$ (pH 8)	Intermediate of glucose-glycogen interconversion	26

Table 2 (continued) Sugar phosphates of importance to mammals

Name	Formula and mol. wt.	Structure	Elementary composition			Specific rotation	Biological function	
			C	H	P			
D-Glucosamine 6-phosphate	$C_6H_{14}NO_8P$ 259.15		27.81	5.45	11.95	$[\alpha]_D^{25} + 56^\circ$	Formed from D-glucosamine by yeast enzyme preparations and by hexokinase	1
D-Gluconic acid 6-phosphate	$C_6H_{12}O_{10}P$ 276.14		26.10	4.75	11.22	$[\alpha]_D^{25} + 0.2^\circ$	Intermediate of pentose phosphate cycle	
N-Acetylglucosamine 1-phosphate	$C_8H_{15}NO_8P$ 301.19		31.90	5.35	10.28	$[\alpha]_D^{25} + 79^\circ$	Intermediate in the formation of UDP N-acetylglucosamine and N-acetylneuraminic acid	2
N-Acetylglucosamine 6-phosphate	$C_8H_{15}NO_8P$ 301.19		31.90	5.35	10.28	$[\alpha]_D^{25} + 29.5^\circ$	Intermediate in the formation of N-acetylglucosamine and N-acetylneuraminic acid	31
D-Mannose 6-phosphate (pyranose form)	$C_6H_{12}O_8P$ 260.14		27.70	5.04	11.91	$[\alpha]_D^{25} + 15.1^\circ$	Intermediate of mannose metabolism	31
N-Acetylmannosamine 6-phosphate	$C_8H_{15}NO_8P$ 301.19		31.90	5.35	10.28	$[\alpha]_D^{25} + 11.2^\circ$	Intermediate in biosynthesis of N-acetylneuraminic acid	32
N-Acetylneuraminic acid 9-phosphate	$C_{11}H_{20}NO_{13}P$ 389.26		33.94	5.18	7.96	—	Intermediate in formation of N-acetylneuraminic acid from N-acetylmannosamine	33

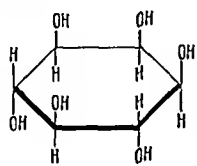
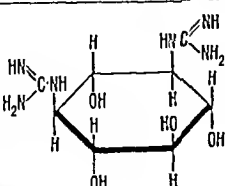
2 (concluded) Sugar phosphates of importance to mammals

Name	Formula and mol wt	Structure	Elementary composition			Specific rotation	Biological function	Reference
			C	H	P			
edoheptulose phosphate	$C_7H_{13}O_{11}P$ 290.17	$\begin{array}{c} CH_2OH \\ \\ CO \\ \\ HOCH \\ \\ HCOH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OPO_3H_2 \end{array}$	28.98	5.21	10.67	—	Intermediate of pentose phosphate cycle	24
edoheptulose 1,7-diphosphate	$C_7H_{13}O_{11}P_2$ 370.15	$\begin{array}{c} CH_2OPO_3H_2 \\ \\ CO \\ \\ HOCH \\ \\ HCOH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OPO_3H_2 \end{array}$	22.71	4.36	16.74	—	Intermediate of pentose phosphate cycle	25
ctose 1-phosphate	$C_{12}H_{22}O_{14}P$ 422.28	 <p>(probable structure)</p>	34.13	5.49	7.33	$[\alpha]_D^{20} + 92.5^\circ$	Possible intermediate in lactose synthesis. Formed from UDP galactose and glucose 1-phosphate	26

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- ⁶ NEUBERG and LUSTIG, *Arch. Biochem.*, **1**, 311 (1942); BELLON and FISCHER, *Abstr. Chem. Soc. 126th Meeting*, 1954, page 70.
- ⁷ NEUBERG and BLOM, *Biochem. Z.*, **301**, 135 (1939).
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- ⁹ NEUBERG et al., *Arch. Biochem.*, **3**, 33 (1944); TANNO, B., *Abstracts of the Communications of the 1st International Congress of Biochemistry*, Cambridge, 1949, page 222.
- ¹⁰ SABLE, H. Z., in BARR et al. (Eds.), *Biochemical Preparations*, vol. 2, Wiley, New York, 1952, page 52.
- ¹¹ KOSTERLITZ, H. W., *Biochem. J.*, **37**, 318 (1943); HANSEN et al., in WESTERFELD et al. (Eds.), *Biochemical Preparations*, vol. 4, Wiley, New York, 1955, page 1.

Table 3 Polyhydric alcohols of importance to mammals

Name	Formula and mol. wt.	Structure ^a	Specific rotation	Occurrence
Glycerol	$C_3H_8O_3$ 92.10	$\begin{array}{c} CH_2OH \\ \\ HCOH \\ \\ CH_2OH \end{array}$	—	Wide occurrence in lipids of mammal tissues. Sweet taste. Component of walls of many GRAM-positive bacteria
Erythritol	$C_4H_{10}O_4$ 122.12	$\begin{array}{c} CH_2OH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OH \end{array}$	Inactive	Isolated from human urine ³
Ribitol (adonitol)	$C_5H_{12}O_6$ 152.15	$\begin{array}{c} CH_2OH \\ \\ HCOH \\ \\ HCOH \\ \\ HCOH \\ \\ CH_2OH \end{array}$	—	Component of riboflavin (vitamin B ₂ , page 472). Also found in <i>Adonis vernalis</i> . Component of cell walls of many GRAM-positive bacteria ⁴
L-Arabitol	$C_6H_{14}O_6$ 152.15	$\begin{array}{c} CH_2OH \\ \\ HCOH \\ \\ HOCH \\ \\ HOCH \\ \\ CH_2OH \end{array}$	$[\alpha]_D - 7.2$	Isolated from human urine in pentosuria
Sorbitol (D-glucitol)	$C_6H_{14}O_6$ 182.17	$\begin{array}{c} CH_2OH \\ \\ HCOH \\ \\ HOCH \\ \\ HCOH \\ \\ CH_2OH \end{array}$	$[\alpha]_D - 1.8$	Constituent of seminal plasma in many species including man
Myoinositol ² (meso-inositol)	$C_6H_{12}O_6$ 180.16		Inactive	Widely distributed in plant and animal kingdoms. Found both free and combined in muscle, heart, liver and other tissues. Component of brain cephalin. The hexaphosphate (phytin) is the organic phosphorus reserve material of green plants. (See also page 491)
Streptidine	$C_8H_{16}N_4O_4$ 262.27		—	Component of streptomycin

References

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ble 4 Oxidation products of carbohydrates

Name	Formula and mol wt	Structure	Specific rotation	Occurrence
<i>Aldonic acids</i>				
D-Glyceric acid (D-α,β-dihydroxypropionic acid)	$C_3H_5O_4$ 106.08		—	As phosphate esters (see Table 2, page 317) which are intermediates in glycolysis
Ascorbic acid (L-xyloascorbic acid, vitamin C)	$C_6H_8O_6$ 176.13		$[\alpha]_D^{25} + 49^\circ$	See under 'Vitamins', page 489
D-Gluconic acid (dextronic acid)	$C_6H_{12}O_7$ 196.16		$[\alpha]_D^{25} - 6.7^\circ \rightarrow +17.5^\circ$	As phosphate ester (see Table 2, page 320), intermediate in pentose phosphate cycle
<i>Uronic acids</i>				
α-D-Galacturonic acid	$C_6H_{10}O_7$ 194.14		$[\alpha]_D^{25} + 100^\circ \rightarrow +68^\circ$	Main component of pectins. Also occurs in some plant gums and mucilages and bacterial polysaccharides (see Table 6, pages 325 and 328)
β-D-Glucuronic acid	$C_6H_{10}O_7$ 194.14		$[\alpha]_D^{25} + 12^\circ \rightarrow +36^\circ$	Component of mucopolysaccharides (see Table 6, pages 325, 327 and 328). Many aliphatic and aromatic hydroxy compounds and acids are excreted as glucuronides (see also page 442). Has pyranose form in natural products.
L-Iduronic acid	$C_6H_{10}O_7$ 194.14		—	Component of chondroitin sulphate B (see Table 6, page 326)

References: 1. TAYLOR, R.S., *Advan. Carbohydr. Chem.*, 9, 185 (1954); WILLIAMS, R.T., *Detoxication Mechanisms*, 2nd ed., Chapman & Hall, London, 1959.

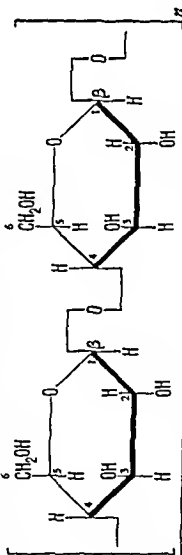
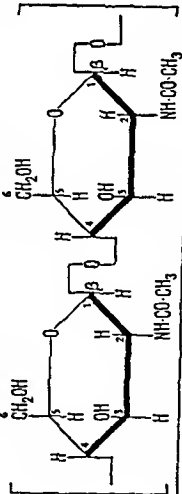
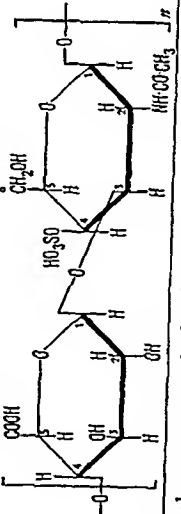
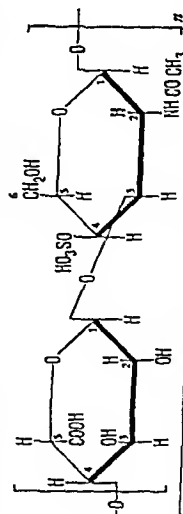
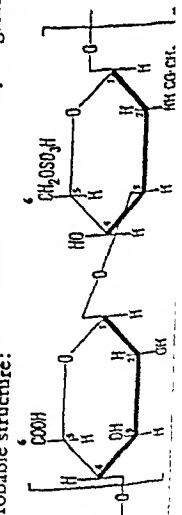
Table 5 Oligosaccharides of importance to mammals¹

Name	Formula and mol. wt.	Structure	Specific rotation	Remarks
<i>Disaccharides</i>				
Cellobiose (4'-[β-D-glucopyranosido]-β-D-glucopyranose)	$C_{12}H_{22}O_{11}$ 342.30		$[\alpha]_D^{20} + 14.2^\circ \rightarrow + 34.6^\circ$	Breakdown product of cellulose arising in herbivores in the course of digestion. Component also of lichenin
Lactose (4'-[β-D-galactopyranosido]-β-D-glucopyranose)	$C_{12}H_{22}O_{11}$ 342.30		α-form, 1 H ₂ O: $[\alpha]_D^{20} + 85^\circ \rightarrow + 52.6^\circ$ β-form: $[\alpha]_D^{20} + 34.9^\circ \rightarrow + 55.4^\circ$	Constituent of mammalian milk (4-8%). Only faintly sweet
Maltose (4'-[α-D-glucopyranosido]-β-D-glucopyranose)	$C_{12}H_{22}O_{11}$ 342.30		β-form, 1 H ₂ O: $[\alpha]_D^{20} + 111.7^\circ \rightarrow + 130.4^\circ$	Breakdown product of starch and glycogen arising in the course of digestion. Found free in some plants (barley) and in honey
Sucrose (saccharose, cane sugar, beet sugar, α-D-glucopyranosido-β-D-fructofuranoside)	$C_{12}H_{22}O_{11}$ 342.30		$[\alpha]_D^{20} + 66.53^\circ$	Almost universal occurrence in the vegetable kingdom
<i>Triaccharide</i>				
Fucosidolactose (2'-[α-L-fucopyranosido]lactose)	$C_{13}H_{24}O_{13}$ 488.44		-	Occurs in traces in human milk along with other di-, tri-, penta- and hexasaccharides ²

Table 6 Polysaccharides of significance in nutrition

name	Mol. wt.	Structure	Specific rotation	Remarks	References
Amorphin (a amylose, B fraction of starch)	Up to 52×10^6 for potato amylopectin		$[\alpha]_D^{20} + 150^\circ$	Main constituent of starch (usually ca. 80%)	1-2
Amylose (B-amylose, A-fraction of starch)	(323), up to 1×10^6		$[\alpha]_D^{20} + 220^\circ$	Constituent of starch (ca. 20%). Absent in some starches, e.g., that of 'waxy' maize (corn)	1-2
Bacterial capsule polysaccharides	-		-	Specific oligosaccharide units of the capsular polysaccharides are responsible for the specific antigenic properties of each bacterial type	9, 10, 12
Bacterial cell-wall polysaccharides (mureins)	-		-	Found particularly in GRAM-positive bacteria, in smaller amount also in some GRAM-negative bacteria	10, 11

Table 6 (continued) Polysaccharides of importance to mammals (for references see page 328)

Name	Mol. wt.	Structure	Specific rotation	Remarks	References
Cellulose	(323) ⁿ , up to 1.7×10^6	Linear chain of β -1,4-linked glucose residues: 	-	Chief structural polysaccharide of plants. Also found in algae, bacterial membranes, and as tunicin in some lower animals. Not digested by man	3
Chitin	(203.19) ⁿ , ca. 4×10^5	Linear chain of β -1,4-linked N-acetyl-D-glucosamine residues: 	$[\alpha]_D^{20} - 14.7^\circ$ (in HCl)	Skeletal substance of molluscs and insects. Also found in lower plants and fungi	4
Chondroitin sulphate A (chondroitin 4-sulphate)	Polydisperse	Polymer composed of D-glucuronic acid, N-acetyl-D-galactosamine and sulphate residues. Probable structure: 	$[\alpha]_D - 28^\circ$ to -32°	Present in mammalian cartilaginous tissue	5, 6
Chondroitin sulphate B (β -heparin, dermatan sulphate)	Polydisperse	Polymer composed of L-iduronic acid, N-acetyl-D-galactosamine and sulphate residues. Probable structure: 	$[\alpha]_D - 60^\circ$ to -32°	Present in mammalian cartilaginous tissue	5, 6
Chondroitin sulphate C (chondroitin 6-sulphate)	Polydisperse	Polymer composed of D-glucuronic acid, N-acetyl-D-galactosamine and sulphate residues. Probable structure: 	$[\alpha]_D - 16^\circ$ to -22°	Present in mammalian cartilaginous tissue	5, 6

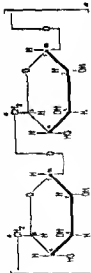
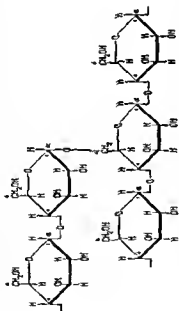
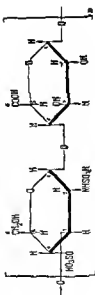
Dextran	(32) ₁₀ ca. 4×10^6	Probably α-1,6-linked glucose residues in branched or straight chains, for instance 			Produced extracellularly by bacteria, e.g. <i>Leuconostoc mesenteroides</i> . Partially degraded dextrans are used as blood-plasma substitutes	2, 2, 2
Glycogen (liver starch)	Polydisperse, for most glycogens at least 2×10^6	Highly-branched molecule resembling amylopectin and containing of unit chains of α-1,4-linked glucose residues interlinked by α-1,6-glycosidic bonds 	[α] _D ²⁰ ca. + 200° (white)		Reserve carbohydrate of animal tissues. Converted in muscle to lactic acid during glycolysis (see page 389). Also present in yeast. Has been synthesized by action of heart or liver phosphorylase on glucose 1-phosphate	2, 2, 2
Glycoproteins	-	Protein containing covalently bound carbohydrate residues other than uronic acids. The carbohydrates are D-glucose, D-mannose, D-glucosamine, D-galactosamine, L-glucose and valine acid; some plant glycoproteins contain also arabinose and xylose. The carbohydrate content ranges from 2-5% in γ-G-globulin up to 15% in the blood-group substances. In many glycoproteins aspartic acid serves as the linking residue between the protein and carbohydrate moieties. In ovomucoid, transferrin, fibrinogen and ovalbumin there seems to be a common structure consisting of (a) a core of D-mannose and D-glucosamine, the latter linked to aspartic acid, and (b) an outer envelope containing D-galactose, L-fucose and in some cases sialic acid	-		Widely distributed in nature. The majority of plasma proteins, many milk and egg proteins, mucins, connective tissue components, hormones and a number of enzymes (bovine pancreatic ribonuclease, horse serum cholinesterase, human serum alkaline phosphatase) have been characterized as glycoproteins	12
Heparin	ca. 17 000	Polymer composed of D-glucosamine, D-glucuronic acid and sulphate residues. Probable structure: 	-		Occurs in animal tissues. Blood anticoagulant	2, 2

Table 6 (continued) Polysaccharides of importance to mammals

Name	Mol. wt.	Structure	Specific rotation	Remarks	Reference
Hyaluronic acid	ca. 1×10^6		—	Widely distributed in tissues and inter-cellular fluids	5, 6
Inulin	(162.14) _n , ca. 5000	<p>Linear chain of about 30 β-1,2-linked fructofuranose units:</p>	$[\alpha]_D^{20} - 40^\circ$	Reserve carbohydrate of many plants, alone or with starch	3
Keratan sulphate (kerato-sulphate)	Polydisperse	<p>Polymer composed of D-galactose, N-acetyl-D-glucosamine and sulphate residues. It is probably (1 \rightarrow 3)-O-β-D-galactopyranosyl-(1 \rightarrow 4)-2-acetamido-2-deoxy-6-O-sulpho-β-D-glucopyranose</p>	—	Originally isolated from the bovine cornea. Occurs in animal connective tissues, e.g., nucleus pulposus, costal cartilage	6
Pectic acid (pectins)	(346) _n , up to 5×10^4	<p>Probably a linear chain of α-1,4-linked D-galacturonic acid residues:</p>	$[\alpha]_D^{20}$ ca. + 240°	Important cell-wall constituent of plants. Occurs as Ca salt or methyl ester	8
Teichoic acids	—	<p>Linear polymers of either glycerol or ribitol phosphate subunits connected in 1,3- or 1,5-phosphodiester linkages respectively. The hydroxyl groups of the polyol monomers may be substituted with D-alanine in an ester bond and with different glycosidically linked mono- or oligosaccharides functioning as the determinant groups of the teichoic acid antigens</p>	—	In cell walls of some bacteria (e.g., <i>Staphylococcus aureus</i>), where the teichoic acid is covalently bound to the muropolysaccharide strands of murein	11

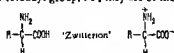
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Constituents of Living Matter – Amino Acids

Amino acids¹

An amino acid is any compound containing one or more amino groups and one or more carboxylic acid groups. Those of biological importance generally contain an amino group in the α -position to a carboxyl group, i.e., they are of the general structure



The asymmetry about the α -carbon atom renders the amino acids optically active, except when $\text{R} = \text{H}$, as in glycine. Their nomenclature is similar to that adopted for the carbohydrate series and involves the use of the small capital letters D and L to indicate

proteins is referred to simply as the L-isomer. This is not, of

The majority of amino acids are stable compounds and melt above 200°C with decomposition; they are insoluble in the common neutral solvents except water, and can usually be recrystallized from aqueous ethanol. Their salt-like behaviour can be ascribed to their existence as internal salts, or 'zwitterions' (see above).

The amino acids behave as amphoteric compounds and possess characteristic isoelectric points, many of their physical properties exhibit maxima and minima at these points.

Amino acid analysis may be carried out by adsorption chromatography on silica gel, partition chromatography on silica gel and paper, ion-exchange chromatography, electrophoresis, thin-film chromatography, and vapour phase chromatography^{2,3}. A single ion-exchange column is now sufficient for the separation of all the common amino acids and an automatic analyser based on this procedure is now commercially available. Many methods exist for the quantitative estimation of amino acids: isotope dilution, enzyme assay, microbial assay and chemical methods⁴.

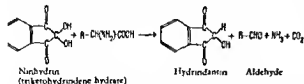
There are three methods of quantitative estimation applicable to the majority of amino acids:

- (1) Amino acids containing a primary amino group react with nitrous acid to give nitrogen.

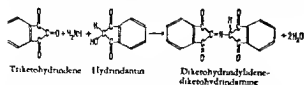


This forms the basis of VAN SLYKE'S method of estimation, the nitrogen being measured volumetrically⁵ or manometrically⁶.

- (2) Amino acids containing free carboxylic and primary α -amino groups are oxidized on heating with ninhydrin



Either NH_3 or CO_2 can be quantitatively measured⁷. Alternatively, the blue colour forming above pH 2 when the reaction mixture is heated, due to the following reaction, can be used for quantitative estimations⁸:



- (3) Formaldehyde reacts with the amino groups of an amino acid and thus reduces their basicity; this allows the acid to be directly titrated with alkali using phenolphthalein as indicator⁹.

constituents of physiologically active compounds.

Polypeptides

Polypeptides are compounds built up of the re



They are derived from amino acids by elimination of water, giving rise to the peptide bond $-\text{HN}-\text{CO}-$ between

soluble readily in aqueous salt solutions, *prolamins*, soluble in alcohol-water mixtures but not in pure alcohol, and various other classes.


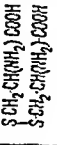
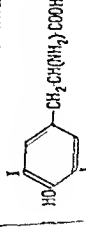
levels of structure is preferable¹¹.

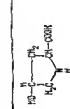
spectrophotometric methods¹².

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Table 7 Physical and chemical properties of amino acids occurring as protein constituents (for references see page 333)

Name	Symbol*	Formula and mol. wt.	Structure	Elementary composition (%)			Solubility (grammes per 100 g water at 25 °C)	Specific rotation				Special properties Organism for microbiological assay	Special occurrence and biological function
				C	H	N		Temp. perature (°C)	Concen- tration**	Solvent	[α] _D		
α-Alanine (α-amino-propionic acid)	Ala	C ₃ H ₇ NO ₂ 89.09	CH ₃ CH(NH ₂)COOH	40.44	7.92	15.72	16.72	25 25 20	2.06 10.00 1.78	6-N HCl Water 3-N NaOH	+ 13.70 + 2.41 + 3.0	<i>Leuconostoc (Lactobacillus) citreorum</i> 8081	-
Arginine (α-amino-δ-guanido- <i>n</i> -valeric acid)	Arg	C ₆ H ₁₃ N ₅ O ₄ 174.20		41.37	8.10	32.16	15	23.3 20 20	1.65 3.48 0.87	6-N HCl Water 0.5-N NaOH	+ 27.58 + 12.5 + 11.8	Basic. Gives SAKAGUCHI color reaction with α-naphthol and sodium hypochlorite <i>Streptococcus faecalis</i> 9790; <i>Leuconostoc citreorum</i>	Intermediate in ornithine cycle of urea synthesis (see pages 442-444) and in creatine synthesis (see pages 437-438)
Asparagine (aspartic acid β-monamide; α-amino-β-carbonyl-propionic acid)	Asn or Asp (NH ₂) Asp NH ₂	C ₄ H ₇ N ₂ O ₅ 132.12	NH ₂ COCH ₂ CH(NH ₂)COOH	36.36	6.10	21.20	2.46	20 20 20	2.24 1.41 11.23	3.4-N HCl Water 2.5-N NaOH	+ 34.26 - 5.30 - 6.35	Hydrolysed by hot acid or specific enzymes to give NH ₃ + aspartic acid	Found in free state in many plant tissues, especially etiolated seedlings
Aspartic acid (amino succinic acid)	Asp	C ₄ H ₇ NO ₄ 133.10	HOOCCH ₂ CH(NH ₂)COOH	36.10	5.30	10.52	0.50	24 18 18	2.02 1.33 1.33	6-N HCl Water 3-N NaOH	+ 24.6 + 4.7 - 1.7	Acidic. Yields 2 moles of CO ₂ and 1 mole of NH ₃ in ninhydrin reaction <i>Leuconostoc mesenteroides</i> P-60, 8042	Involved in transformation of citrulline to arginine (see pages 442-444), and in biosynthesis of purines and pyrimidines (see pages 433 and 438-439)
Cysteine (α-amino-β-thiolpropionic acid)	Cys	C ₃ H ₇ NO ₂ S 121.16	HSCH ₂ CH(NH ₂)COOH	29.74	5.82	11.56	Very soluble	26	12.1	1-N HCl	+ 7.6	Readily autooxidized in neutral or basic solution to cystine	Interconvertible with cystine by oxido-reduction. Component of glutathione (see page 438). Some aromatic compounds are excreted in urine as derivatives of <i>N</i> -acetylcysteine (mercapturic acids) (see page 445)
Cystine (di-(α-amino-propionyl)-β-disulphide)	Cys Cys	C ₆ H ₁₂ N ₂ O ₄ S ₂ 240.30		29.99	5.03	11.66	0.011	24 18.5	1.0 0.4	1-N HCl 0.2-N NaOH	-214.4 - 70.0	Readily reduced to cysteine <i>Leuconostoc mesenteroides</i> P-60, 8042; <i>Lactobacillus arabinosus</i>	Occurs abundantly in hair, keratin and insulin. The disulphide bond links together different polypeptide chains or different parts of the same polypeptide chain within the protein molecule
3,5-Di-iodo-tyrosine**	-	C ₉ H ₉ NO ₄ I ₂ 432.99		24.97	2.10	3.23	0.062	20 20	5.08 4.41	1.1-N HCl 3.4-N NH ₄ OH	+ 2.89 + 2.27	-	Occurrence confined to protein of thyroid gland (thyroid hormones; see page 440)

Glutamic acid (α-amino-glutaric acid)	$C_5H_9NO_4$ 147.15	$HOOC(CH_2)_3CH(NH_2)COOH$	40.22 8.17 9.52	0.843	22.4 11.5 1.47	6-N HCl Water 2-N NaOH	+ 31.2 + 11.5 + 10.96	Acidic. On boiling in solution over a wide pH range (4-10) cyclizes to pyrrolidonecarboxylic acid <i>Leuconine nitrilolactide</i> p-60, 8042; <i>Leuconine nitrilolactide</i>	Component of glutamine (see page 438) and of the false (see page 438) (see page 479). Present in high concentration in tissues. More readily dehydrated to animal tissue than any other amino acid, and also more reactive in enzymic transamination reactions
Glutamine (Glutamic acid β-aminoamide, γ-carbamyl-L-butiric acid)	$C_5H_{11}N_2O_6$ 146.15	$HN(CH_2)_3CH(NH_2)COOH$	41.05 8.90 13.17	3.6 (at 18°C)	22	Water	+ 5.0	On heating in solution to ca 100°C at near neutrality cyclizes to ammonium salt of pyrrolidonecarboxylic acid. Amide group reacts with nitrous acid to produce N-hydroxy-L-glutamic acid. Hydrolyzed by specific enzyme to ammonium glutamate.	Occurs in the free state in animal tissues and many plants, e.g., sugar beet. The pyridine ring is formed by pyridine and phenethylamine (see page 445). Intermediate carrier of amino groups. See also page 434
Glycine (aminoacetic acid)	$C_2H_5NO_2$ 75.07	NH_2CH_2COOH	32.00 6.71 18.66	24.99	-	-	-	Optically inactive. Gives green colour with α-phthalaldehyde <i>Leuconine nitrilolactide</i> p-60, 8042	In many animals benzoic acid is excreted as benzoyl-L-glutamate (see page 444 and 445). Component of glutathione (see page 436). Nucleobases in synthesis of creatine, porphyrins, purines (see page 434). Formed from aspartate in mammals (see page 432)
Histidine (γ-amino-β (4-imidazole)-propionic acid)	$C_6H_7N_3O_2$ 133.16	$HO-CH_2-CH(NH_2)-COOH$	46.45 5.85 27.08	4.29	25 25 20	6-N HCl Water 0.5-N NaOH	+ 13.34 - 58.95 - 10.9	Basic. Gives bluer tint, couples with diazotized α-phthalic acid to give intense red colour (Frost reaction) <i>Leuconine nitrilolactide</i> p-60, 8042	Deacetylated to histamine. Component of the common (β-alanylhistidine) found in muscle
δ-Hydroxylysine (ε-ε-amino-β hydroxy-α-amino acid)	$C_7H_{11}N_3O_4$ 182.17	$NH_2CH_2CH(OH)(CH_2)_3CH(NH_2)COOH$	44.43 8.70 17.27	-	25	6-N HCl	+ 14.5	Reacts with periodate to yield formaldehyde and ammonium	Has been found as proteocon-sultant only in collagen and gelatin. Phosphate ester occurs naturally*
Hydroxyproline (γ-hydroxy-pyrrolidine-α-carboxylic acid)	$C_5H_7NO_3$ 131.15		45.80 6.92 10.68	26.11	20 22.5 20	1-N HCl Water 0.5-N NaOH	- 47.3 - 75.2 - 70.6	Has no primary α-amino group and therefore differs in many respects from primary amino acids, e.g., with aromatic amino acids. Oxidized by hypochlorite to give hydroxyproline. De-carboxylated by anhydride to give reddish colour below pH 4.4, yellowish colour at higher pH. Forms bright blue condensation product with ninhydrin	Component of gelatin, collagen and many other extracellular peptides* See also page 432

* Recommended by the Combined Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the International Union of Pure and Applied Chemistry.

** As gaseous per 100 ml solution unless otherwise stated

*** For chromatographic separation from other isolated amino acids, see examination see BUCK and WATTS*.

Table 7 (continued) Physical and chemical properties of amino acids occurring as protein constituents

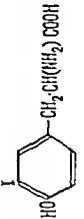

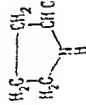



Name	Symbol*	Formula and mol. wt.	Structure	Elementary composition (%)			Solubility (grammes per 100 g. water at 25°C)	Specific rotation			Special properties <i>Organism for microbiological assay</i>	Special occurrence and biological function
				C	H	N		Tem- perature (°C)	Concen- tration**	Solvent		
Leucine (α -amino- isocaproic acid)	Leu	$C_6H_{13}NO_2$ 131.18	$(CH_3)_2CH-CH_2-CH(NH_2)COOH$	54.04	9.99	10.68	2.19	25	2.00	6-N HCl	<i>Lactobacillus arabinosus</i> 17-5, 8014; <i>Lactobacillus helveticus</i> ; <i>Streptococcus faecalis</i> ; <i>Leuconostoc mesenteroides</i> P-60, 8042	-
Isoleucine (α -amino- β -methyl- n-valeric acid)	Ile	$C_6H_{11}NO_2$ 131.18	$CH_3-CH_2-CH(CH_3)-CH(NH_2)COOH$	54.04	9.99	10.68	2.93 (at 20°C)	25 20 20	2.00 3.10 3.34	6-N HCl Water 0.33-N NaOH	<i>Lactobacillus arabinosus</i> 17-5, 8014; <i>Lactobacillus helveticus</i> ; <i>Streptococcus faecalis</i> ; <i>Leuconostoc mesenteroides</i> P-60, 8042	-
Lysine (α , ϵ -diamino- n-caproic acid)	Lys	$C_6H_{12}N_2O_2$ 146.19	$NH_2-(CH_2)_4-CH(NH_2)COOH$	49.30	9.65	19.16	Very soluble	23 20	2.00 6.50	6-N HCl Water	Basic. Can be precipitated with phosphotungstic acid. Dry heating of proteins containing lysine causes an apparent loss of lysine <i>Streptococcus faecalis</i> 9790; <i>Leuconostoc mesenteroides</i> P-60, 8042	-
Methionine (α -amino- γ -methylthio- n-butyric acid)	Met	$C_4H_9NO_2S$ 149.21	$CH_3-S-CH_2-CH_2-CH(NH_2)COOH$	40.25	7.43	9.39 Sulphur 21.49	3.35 (for DL-acid)	20 25	5.00 0.80	3-N HCl Water	<i>Leuconostoc mesenteroides</i> P-60, 8042; <i>Lactobacillus fermenti</i> 36 (for DL-acid)	Provides the sulphur atom for cysteine biosynthesis (see 'Cystathionine', Table 8, page 335). Carrier of 'active' methyl groups
3-Moniodo- tyrosine	-	$C_9H_9NO_3I$ 307.09		35.20	3.28	4.56 Iodine 41.32	-	20	5.00	1-N HCl	-	Occurrence confined to protein of thyroid gland (thyroid hormones; see page 440)
Norleucine (α -aminocaproic acid)	-	$C_6H_{13}NO_2$ 131.18	$CH_3-(CH_2)_4-CH(NH_2)COOH$	54.04	9.99	10.68	1.15 (at 18°C)	20	4.3	6-N HCl	+ 21.3	Has not been proved to be a protein constituent 4
Phenylalanine (α - amino- β -phenyl- propionic acid)	Phe	$C_9H_9NO_2$ 165.19		65.44	6.71	8.48	2.965	20	1.93	Water	- 35.14	Can be converted to tyrosine in the human body (see page 398)
Proline (pyrrolidine- α -carboxylic acid)	Pro	$C_5H_9NO_2$ 115.13		52.16	7.88	12.17	162.3	20 23.4 20	0.57 1.00 2.42	0.5-N HCl Water 0.6-N KOH	- 52.6 - 85.0 - 93.0	Protein constituent. See also page 432 <i>Leuconostoc mesenteroides</i> P-60, 8042; <i>Lactobacillus brevis</i>

Table 8 Physical and chemical properties of some amino acids not occurring in proteins but found in the free form

Name	Formula and mol. wt.	Structure	Elementary composition (%)			Solubility (grammes per 100 g water at 25°C)	Specific rotation			Special properties	Occurrence and biological function
			C	H	N		Temperature (°C)	Concentration (g per 100 ml solution)	Solvent		
β -Alanine (β -amino-propionic acid)	$C_3H_7NO_2$ 89.09	$NH_2-CH_2-CH_2-COOH$	40.44	7.92	15.72	Very soluble	-	-	-	-	Breakdown product of pyrimidines (see page 401). Occurs as constituent of pantothenic acid, coenzyme A, carnosine and anserine. See also page 434
α -Aminoadipic acid	$C_6H_{11}NO_4$ 161.16	$HOOC-(CH_2)_3-CH(NH_2)-COOH$	44.72	6.88	8.69	0.22 (at 20°C)	-	-	-	Decomposes on heating to α -piperidone- α' -carboxylic acid	Intermediate in breakdown of lysine (see page 398)
α -Amino- <i>n</i> -butyric acid	$C_5H_9NO_3$ 103.12	$CH_3-CH_2-CH(NH_2)-COOH$	46.59	8.80	13.58	28 (for DL-acid)	20	5.46	Water	+ 7.86	Found in brain preparations ¹ . Occurs as constituent of tripeptide ophthalmic acid in lens tissue ²
γ -Amino- <i>n</i> -butyric acid	$C_5H_9NO_3$ 103.12	$NH_2-(CH_2)_3-COOH$	46.59	8.80	13.58	-	-	-	-	-	Found in brain ³ , lung and heart ¹ preparations
β -Amino- <i>n</i> -butyric acid	$C_5H_9NO_3$ 103.12	$NH_2-CH_2-CH(CH_3)-COOH$	46.59	8.80	13.58	-	-	-	-	-	Breakdown product of thymine (see page 401)
δ -Aminolaevulinic acid (γ -keto- δ -amino- <i>n</i> -valeric acid)	$C_5H_9NO_3$ 131.13	$NH_2-CH_2-CO-CH_2-CH_2-COOH$	45.80	6.92	10.68	-	-	-	-	-	Intermediate in porphyrin biosynthesis (see page 437)
Argininosuccinic acid	$C_6H_{11}N_3O_6$ 290.28	$HOOC-CH(NH_2)-(CH_2)_2-NH-C(=NH)-CH(NH_2)-COOH$	41.38	6.25	19.30	-	24 24 24	2.9 2.9 2.9	Water 0.5-N NaOH 0.5-N HCl	+ 16.4 + 26.6 + 5.2	Intermediate metabolite in ornithine cycle of urea synthesis ⁴ (see pages 442 and 444). Excreted in the urine of some mental defectives ⁵ (see page 449)
Carbamylaspartic acid (α -amino-ureidosuccinic acid)	$C_5H_8N_2O_6$ 176.13	$HOOC-CH_2-CH(COOH)-NH-CO-NH_2$	34.10	4.58	15.90	0.4 (at 20°C)	25	-	Water (Ba salt)	+ 24.1	Intermediate in biosynthesis of pyrimidines from aspartic acid in mammals and bacteria (see page 439)
Citrulline (α -amino- δ -ureido- <i>n</i> -valeric acid)	$C_5H_{10}N_3O_3$ 175.19	$NH_2-CO-NH-(CH_2)_3-CH(NH_2)-COOH$	41.14	7.48	23.99	-	21 21	5.00 5.00	0.3-N HCl Water	+ 17.9 + 3.5	Intermediate in ornithine cycle of urea synthesis (see pages 442-443)
Creatine (methyl-glycocyamine)	$C_4H_7N_3O_2$ 131.14	$NH_2-C(=NH)-N(CH_3)-CH_2-COOH$	36.64	6.92	32.04	1.35 (at 18°C)	-	-	-	-	Cell constituent. Creatine phosphate acts as store of 'phosphate bond energy' in vertebrate muscle (see page 437)
Creatinine (1-methylglycocyamine)	$C_4H_7N_3O$ 113.12	$NH_2-C(=NH)-N(CH_3)-CH_2-CO$	42.47	6.24	37.15	8.7 (at 16°C)	-	-	-	-	Present in urine

Cystathionine	$C_4H_{11}N_2O_3S$ 222.26	$HO_2C(CH_2)_2CH_2SCH_2CH_2CH_2COOH$	37.81 Sulphur 14.43	6.35 12.60	-	22	1.0	1- α HCl	+ 23.7	-	Intermediate in transamination of methionine with serine (see page 398)
Cysteic acid	$C_3H_7NO_3S$ 169.16	$HO_2CCH_2CH_2COOH$	21.30 Sulphur 18.98	4.17 8.28	-	28	6.0	Water	+ 7.8	-	Intermediate in formation of taurine, a bile constituent (see below), from cysteine
Ergothioneine (basine of thiohistidine)	$C_{11}H_{17}N_3O_3S$ 229.30		47.14 Sulphur 13.98	8.59 18.33	-	21	5.0	Water	+116.0	-	Basic. Stable to alkalis, thiol group is readily oxidized to sulphate under acid conditions. Gives reddish purple colour with diazotized sulphamic acid and alkali.
Glycothionine (β-aminothionine acid)	$C_4H_7N_2O_3$ 117.11	$HO-CH_2CH_2CH_2COOH$	30.77	8.03 35.88	Slightly soluble	-	-	-	-	-	In urine. Formed in kidney from arginine and glycine. Precursor of creatine and creatinine (see page 437)
Homoserine (α-amino-γ-hydroxy-β-butyric acid)	$C_4H_9NO_3$ 119.12	$HOCH_2CH_2CH_2COOH$	40.33	7.62 11.76	-	24 to 28	0.25	5- α HCl	+ 18.5	-	Intermediate in methionine and homocysteine metabolism (see pages 397-398)
1-Methylthioline (2-aminomethylamine)	$C_5H_{11}N_2O_3$ 169.18		49.70	6.55 24.84	20	18	3.72	Water	- 26	-	Free acid isolated from normal urine ⁷ . In combination with β-alanine forms the dipeptide anisetone found in animal muscle ⁸
3-Methylthioline	$C_5H_{11}N_2O_3$ 169.18		49.70	8.55 24.84	-	26	-	Water	- 25.4 - 26.5	-	Isolated from normal urine ⁹
Ornithine (2-aminomethylamine acid)	$C_4H_9N_2O_3$ 132.15	$H_2N(CH_2)_3CH_2COOH$	45.44	9.15 21.20	Very soluble	20	0.84	0.45- α HCl	+ 14.1	-	Intermediate in ornithine cycle of urea synthesis (see pages 442-443). Benzoinic acid is excreted by the fowl as N,N' -dibenzoylornithine
Taurine (2-aminoethanesulphonic acid)	$C_2H_7NO_3S$ 125.15	$H_2NCH_2CH_2SO_3H$	19.20 Sulphur 25.62	5.64 11.19	8.78 (at 20°C)	-	-	-	-	-	In muscle tissue of invertebrates. Formed in mammalian liver from cysteine (see page 438). Component of taurocholic acid (bile acid)

References

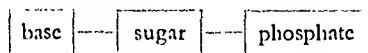
- ¹ RAYNER, D. M., *Biochem. J.*, 52, 679 (1952)
- ² WATERS, S. G., *Biochem. J.*, 44, 715 (1950)
- ³ UNANUE, S. J., *Biol. Chem.*, 187, 65 (1950)
- ⁴ RAYNER, D. M., *J. Biol. Chem.*, 204, 95 (1953)
- ⁵ WATKINS, K. G., *Biochem. J.*, 77, 135 (1960)
- ⁶ For review see BENT, D. J., *Adv. Exp. Phys. Chem.*, 52, 285 (1953)
- ⁷ STALLER and WATKINS, *Biochem. J.*, 46, 1 (1951)
- ⁸ LLOYD, C. (Ed.), *Biochem. J.*, 52, 638 (1952); TALLAN et al., *J. Biol. Chem.*, 206, 825 (1954)
- ⁹ WATKINS, K. G., *Biochem. J.*, 52, 638 (1952); TALLAN et al., *J. Biol. Chem.*, 206, 825 (1954)

Nucleosides and nucleotides

A *nucleoside* is a sugar linked to a heterocyclic base. A *nucleotide* is a nucleoside in which the sugar is esterified with phosphoric acid.

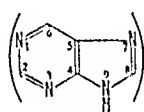
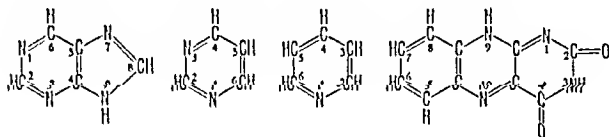


Nucleoside



Nucleotide

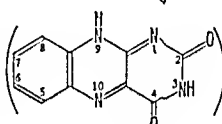
The bases found in nucleosides and nucleotides are most commonly purines and pyrimidines. Others include pyridines and isoalloxazines. The parent compounds of these bases are:



Purine

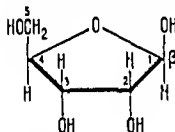
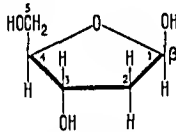
Pyrimidine
(1,3-diazine)

Pyridine

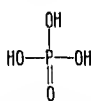
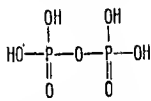
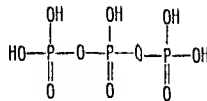


Isoalloxazine

The sugars found in nucleosides and nucleotides are most commonly either ribose or 2-deoxyribose:

Ribose
(β-D-ribofuranose)2-Deoxyribose
(β-D-2-deoxyribofuranose)

The base-glycoside linkage of nucleosides and nucleotides occupies the 9-position in the case of purines and the 3-position in the case of pyrimidines. Esterification of nucleosides is not confined to orthophosphoric acid. It occurs also with pyrophosphoric (diphosphoric) acid and triphosphoric acid.

Orthophosphoric acid
(monophosphoric acid)Pyrophosphoric acid
(diphosphoric acid)

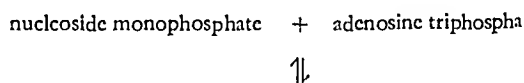
Triphosphoric acid

The nomenclature of the nucleosides and nucleotides is stated by the examples given in Table 9 opposite.

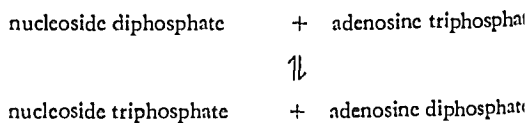
The naturally occurring nucleoside mono-, di- and triphosphates have the sugar-phosphate ester linkage in the 5'-position. The naturally occurring nucleoside 3'-monophosphates and the naturally occurring nucleoside 3',5'-diphosphates formed during enzymatic digestion of nucleic acids. In the case of certain coenzymes, a nucleoside diphosphate or nucleoside 3',5'-diphosphate structure is encountered (see Table 12, pages 344–350).

Nucleotides and polynucleotides (see Nucleic acids, page 354) occur in all living cells. Certain naturally occurring nucleosides and nucleotides have no known function apart from being intermediates in the synthesis or breakdown of nucleotides (Tables 10a, b, c, pages 338–342).

Nucleoside di- or triphosphates are precursors of the nucleic acids. They act also as carriers of the free energy of pyrophosphate bonds. In this capacity, nucleotides may be regarded as coenzymes of the free-energy transfer that occurs in many synthetic and degradative reactions. Nucleoside diphosphates are formed from nucleoside monophosphates by nucleoside monophosphate kinase. This enzyme is analogous in action to adenosine kinase and catalyses the general reaction¹:



Nucleoside triphosphates are formed in turn from the corresponding diphosphates by nucleoside diphosphate kinase¹:



A list of nucleoside mono-, di- and triphosphates and their functions is given in Table 11, page 343.

The nucleotide coenzymes act as carriers of hydrogen atoms (hydrogenases) and as carriers of the active forms of sugars, acids, fatty acids, dicarboxylic acids, carbon dioxide, and sulfur. The roles and modes of formation of nucleotide coenzymes are listed in Table 12, pages 344–350.

References

- ¹ LIEBERMAN et al., *J. biol. Chem.*, **215**, 429 (1955); GIBSON et al., *Biochim. phys. Acta (Amst.)*, **21**, 86 (1956).

4.9 Nomenclature of nucleosides and nucleotides

The group names are the names which can be applied to any compound of the type shown. In general the terms nucleoside and nucleotide are

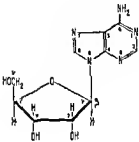
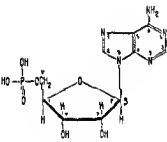
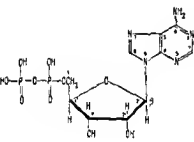
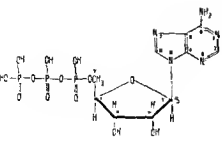
Structural formula	Group name	Alternative group name	Specific name	Specific alternatives
	Nucleoside	Ribonucleoside (ribosylbase)	Adenosine	Ribosyladenine
	Nucleotide (nucleoside mono-phosphate)	Ribonucleotide (ribosylbase mono-phosphate)	5'-Adenylic acid (AMP)	Adenosine 5'-phosphate (adenosine monophosphate) Adenine nucleotide Ribosyladenin 5'-phosphat
	Nucleoside diphosphate	Ribosylbase diphosphate	Adenosine diphosphate (ADP)	Adenosine 5'-pyrophosphate
	Nucleoside triphosphate	Ribosylbase triphosphate	Adenosine triphosphate (ATP)	

Table 10a Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Purines and pyrimidines

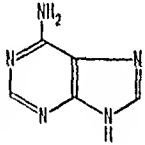
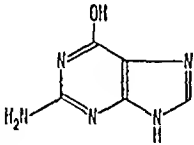
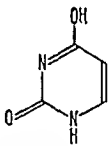
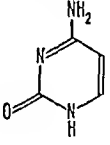
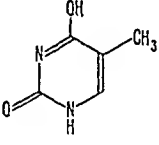
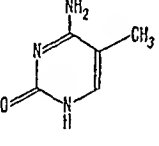
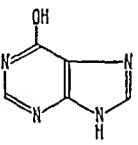
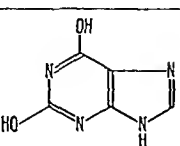
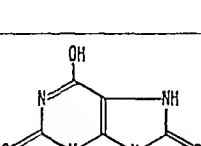
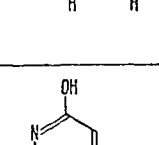
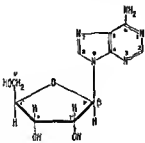
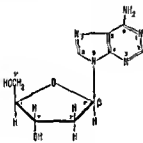
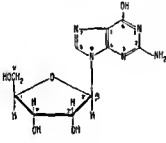
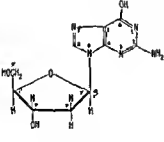
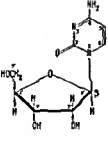
Name	Formula and mol.wt.	Structure	Properties	Occurrence	Function
Adenine (6-amino-purine)	$C_5H_5N_9$ 135.13		m.p. 365 °C (decomp.); picrate 298 °C	Occurs in tea, sugar beet, yeast, various animal organs	These bases are the products of the degradation of the corresponding nucleotides. They are further degraded by the pathway shown on pages 399–400. In mammals only adenine can be converted back to the corresponding nucleotide under normal conditions but the extent to which this occurs is uncertain.
Guanine (2-amino-6-hydroxy-purine)	$C_5H_5N_9O$ 151.13		m.p. 365 °C (decomp.); picrate 258–260 °C	Occurs in scales and flesh of fish	
Uracil (2,6-dihydroxypyrimidine)	$C_4H_4N_2O_2$ 112.09		m.p. 338 °C (decomp.)	–	
Cytosine (6-amino-2-hydroxypyrimidine)	$C_4H_5N_3O$ 111.10		m.p. 320–325 °C (decomp.); picrate 333 °C	–	
Thymine (2,6-dihydroxy-5-methyl-pyrimidine)	$C_5H_8N_2O_2$ 126.12		m.p. 321–325 °C	–	
5-Methylcytosine (5-methyl-6-amino-2-hydroxypyrimidine)	$C_5H_8N_3O$ 125.13		m.p. 270 °C (decomp.); picrate 290–291 °C	Occurs in calf thymus nucleic acid and wheat germ deoxyribonucleic acid	–
Hypoxanthine (6-hydroxypurine)	$C_5H_4N_4O$ 136.11		m.p. 150 °C (decomp.); picrate 246 °C	Occurs in muscle, meat extracts, blood, urine (the latter especially in leukaemia)	Product of deamination of adenine; precursor of xanthine
Xanthine (2,6-dihydroxypurine)	$C_5H_4N_4O_2$ 152.11		m.p. 262–264 °C (perchlorate)	Occurs in small quantities in plants, blood, liver, urine, yeast. Component of butterfly pigments and rare urinary calculi	Formed by oxidation of hypoxanthine, or by deamination of guanine; precursor of uric acid
Uric acid (2,6,8-trihydroxypurine)	$C_5H_4N_4O_3$ 168.11		m.p. > 400 °C (decomp.) d^{20}_D 1.836	Occurs in urine and renal and urinary calculi (increased in urine and blood in gout, leukaemia, nephritis, pneumonia). Also in faeces of birds and reptiles	Formed by oxidation of xanthine. Chief product of nitrogen excretion in reptiles and birds. In mammals other than primates further degraded to allantoin (see page 400)
Orotic acid (2,6-dihydroxypyrimidine-4-carboxylic acid)	$C_5H_4N_2O_4$ 156.10		m.p. 345–347 °C (decomp.); ethyl ester 200 °C	Occurs in milk	Precursor of orotidylic acid (see pages 438–439)

Table 10b Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Nucleosides

 The purine nucleosides listed in this table all contain 9-N β -ribose or -deoxyribose linkages, the pyrimidine nucleosides 3-N β -ribose or -deoxyribose linkages. For explanation of the nomenclature see Table 9, page 337.

Name*	Formula and mol. wt	Structure	Specific rotation	Function in mammalian tissue
Adenosine (Ado, A) (ribosyladenine)	$C_{10}H_{12}N_5O_4$ 267.25		$[\alpha]_D^{20} - 67.3^\circ$ (0.1-N NaOH)	
Deoxyadenosine (deoxyribosyl- adenine)	$C_{10}H_{11}N_5O_3$ 251.25		$[\alpha]_D^{20} - 26^\circ$	
Guanosine (Guo, G) (ribosylguanine)	$C_{10}H_{12}N_5O_4$ 263.25		$[\alpha]_D^{20} - 60^\circ$ (2% solution)	These nucleosides are products of the enzymic hydrolysis of the corresponding 3'- or 5'-nucleotides. The nucleosides in turn are broken down further by phosphorolysis yield ribose 1-phosphate, deoxyribose 1-phosphate at the corresponding base. Nucleoside kinases that form nucleotides from nucleoside plus ATP are known to occur in yeast and in some animal tissues. Their importance in mammals has not as yet been assessed.
Deoxyguanosine (deoxyribosyl- guanine)	$C_{10}H_{11}N_5O_3$ 267.25		$[\alpha]_D^{20} - 47.7^\circ$ (1-N NaOH)	
Cytidine (Cyd, C) (ribosylcytosine)	$C_9H_{12}N_4O_4$ 243.22		$[\alpha]_D^{20} + 29.6^\circ$	

* The three-letter symbols are those recommended by the Combined Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the International Union of Biochemistry (J Biol

Chem, 241, 527 [1966]). Other symbols are Tld or T for ribosylthymine; Tld or T for 3-ribosylthymine (pseudouridine). Deoxy compounds are indicated by the prefix d (for example dAdo or dA for deoxyadenosine).

Table 10b (continued) Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Nucleosides

Name*	Formula and mol.wt.	Structure	Specific rotation	Function in mammalian t
Deoxycytidine (deoxyribosyl-cytosine)	$C_9H_{13}N_3O_4$ 227.22		$[\alpha]_D^{25} + 40^\circ$	
Uridine (Urd, U) (ribosyluracil)	$C_9H_{12}N_2O_6$ 244.21		$[\alpha]_D^{25} + 9.6^\circ$	These nucleosides are products of the enzymic hydrolysis of the corresponding 3', 5'-nucleotides. The nucleosides in turn are broken down further by phosphorolysis to yield ribose 1-phosphate and deoxyribose 1-phosphate and the corresponding base. Nucleoside kinases that form nucleotides from nucleosides plus ATP are known to occur in yeast and in some animal tissues. Their importance in mammals has not at present been assessed
Deoxythymidine (deoxyribosyl-thymine)	$C_{10}H_{14}N_2O_6$ 242.23		$[\alpha]_D^{25} + 32.50^\circ$ (1-N NaOH)	
Inosine (Ino, I) (ribosyl-hypoxanthine)	$C_{10}H_{12}N_4O_6$ 268.23		$[\alpha]_D^{25} - 72.45^\circ$ (0.1-N NaOH)	

* See footnote page 339.

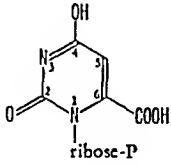
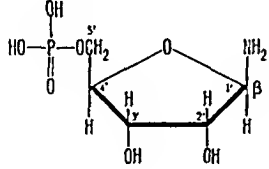
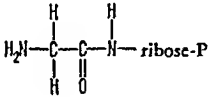
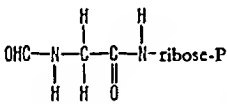
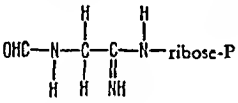
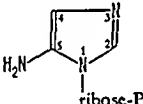
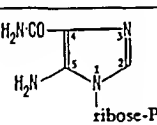
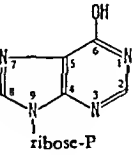
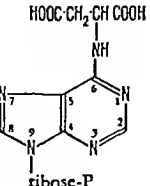
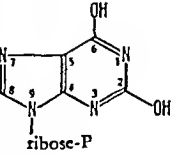
Constituents of Living Matter - Nucleosides and Nucleotides

Table 10b (concluded) Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleosides; Nucleosides

Name*	Formula and mol. wt.	Structure	Specific rotation	Function in mammalian cells
Deoxyinosine (deoxyribosyl-hypoxanthine)	$C_{10}H_{13}N_5O_4$ 252.23		$[\alpha]_D^{25} - 22.9^\circ$ (1-N NaOH)	
Xanthosine (Xao, X) (ribosylxanthine)	$C_{10}H_{13}N_5O_5$ 284.23		$[\alpha]_D^{25} - 51.21^\circ$	These nucleosides have known function either their role as intermediates in the synthesis or breakdown of nucleosides (see page 40)
Deoxyxanthosine (deoxyribosyl-xanthine)	$C_{10}H_{13}N_5O_4$ 268.23		-	
Ribosyluric acid	$C_{10}H_{13}N_5O_7$ 300.23		$[\alpha]_D^{25} - 40.8^\circ$ (0.1-N NaOH)	

* See footnote page 339

Table 10: Compounds involved in the biosynthesis and breakdown of purine and pyrimidine nucleotides: Nucleotides
 With the exception of inosinic acid, the compounds listed here have no known coenzyme activity.

Name	Formula and mol.wt.	Structure*	Function
Orotidylic acid (OMP) (ribosylorotic acid 5'-phosphate)	$C_{10}H_{13}N_4O_{11}P$ 368.20		Intermediate in biosynthesis of pyrimidine nucleotides. Formed from orotic acid (see pages 438–4)
5-Phosphoribosyl-amine (D-ribosylamine 5'-phosphate)	$C_5H_{10}NO_7P$ 229.13		Intermediates in biosynthesis of inosinic acid (s pages 433 and 435)
Ribosylglycinamide 5'-phosphate	$C_7H_{14}N_4O_8P$ 286.18		
Ribosylformyl-glycinamide 5'-phosphate	$C_8H_{15}N_5O_8P$ 314.19		
Ribosylformyl-glycinamidine 5'-phosphate	$C_8H_{15}N_5O_8P$ 313.21		
1-Ribosyl-5-amino-imidazole 5'-phosphate	$C_8H_{13}N_5O_7P$ 295.19		
1-Ribosyl-5-amino-imidazole-4-carboxamide 5'-phosphate	$C_9H_{14}N_6O_8P$ 338.22		
Inosinic acid (IMP) (inosine 5'-phosphate)	$C_{10}H_{13}N_4O_8P$ 348.21		Precursor of adenosine 5'-phosphate (AMP) and guanosine 5'-phosphate (GMP) (see Table 11, page 343). Can partially replace certain coenzyme functions of other nucleotides
Succinyladenylic acid (succinyl-adenosine 5'-phosphate)	$C_{14}H_{18}N_6O_{11}P$ 463.30		Intermediate in synthesis of adenosine 5'-phosphate (AMP) from inosinic acid (see pages 435–436)
Xanthylic acid (XMP) (xanthosine 5'-phosphate)	$C_{10}H_{13}N_4O_8P$ 364.21		Intermediate in synthesis of guanosine 5'-phosphate (GMP) from inosinic acid (see page 436)

* For structure of the 'ribose-P' portion of the molecule see Table 9, page 337.

Constituents of Living Matter - Nucleotides

Table 11 Nucleoside 5'-mono-, di- and triphosphates (5'-nucleotides)

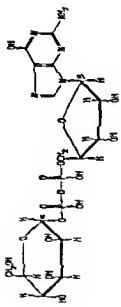
Name	Abbreviation	Formula	Mol. wt.	Function
Adenosine monophosphate (adenylic acid)	AMP	$C_{10}H_{12}N_4O_7P$	347.23	Precursor of ADP. Activates phosphoryla
Adenosine diphosphate	ADP	$C_{10}H_{12}N_4O_8P_2$	427.21	Immediate precursor of polynucleotides. other functions see page 404
Adenosine triphosphate	ATP	$C_{10}H_{12}N_4O_{10}P_3$	507.19	Precursor of adenosine coenzymes (see Table pages 344-346). For other functions see page
Deoxyadenosine monophosphate	dAMP	$C_{10}H_{14}N_4O_7P$	331.23	Precursor of deoxyadenosine diphosphate
Deoxyadenosine diphosphate	dADP	$C_{10}H_{14}N_4O_8P_2$	411.21	Precursor of deoxyadenosine triphosphate
Deoxyadenosine triphosphate	dATP	$C_{10}H_{14}N_4O_{10}P_3$	491.19	Immediate precursor of deoxyribopolynuc
Guanosine monophosphate (guanylic acid)	GMP	$C_9H_{12}N_4O_7P$	363.23	Precursor of guanosine diphosphate
Guanosine diphosphate	GDP	$C_9H_{12}N_4O_8P_2$	443.21	Immediate precursor of polynucleotides. Yn guanosine triphosphate during cleavage of i ceryl-coenzyme A
Guanosine triphosphate	GTP	$C_9H_{12}N_4O_{10}P_3$	523.19	Precursor of guanosine coenzymes (see T 12, page 347). Formed from orthophosph and guanosine diphosphate during cleavage; succinyl-coenzyme A
Deoxyguanosine monophosphate (deoxyguanylic acid)	dGMP	$C_{10}H_{14}N_4O_7P$	347.23	Precursor of deoxyguanosine diphosphate
Deoxyguanosine diphosphate	dGDP	$C_{10}H_{14}N_4O_8P_2$	427.21	Precursor of deoxyguanosine triphosphate
Deoxyguanosine triphosphate	dGTP	$C_{10}H_{14}N_4O_{10}P_3$	507.19	Immediate precursor of deoxyribopolynuc
Cytidine monophosphate (cytidylic acid)	CMP	$C_9H_{12}N_4O_7P$	323.20	Precursor of cytidine diphosphate
Cytidine diphosphate	CDP	$C_9H_{12}N_4O_8P_2$	403.18	Immediate precursor of polynucleotides. Precursor of cytidine triphosphate
Cytidine triphosphate	CTP	$C_9H_{12}N_4O_{10}P_3$	483.16	Precursor of cytidine coenzymes (see Table pages 349-350)
Deoxycytidine monophosphate (deoxycytidylic acid)	dCMP	$C_9H_{14}N_4O_7P$	307.20	Precursor of deoxycytidine diphosphate
Deoxycytidine diphosphate	dCDP	$C_9H_{14}N_4O_8P_2$	387.18	Precursor of deoxycytidine triphosphate
Deoxycytidine triphosphate	dCTP	$C_9H_{14}N_4O_{10}P_3$	467.16	Immediate precursor of deoxyribopolynuc
Uridine monophosphate (uridylic acid)	UMP	$C_9H_{12}N_2O_7P$	324.19	Precursor of uridine diphosphate
Uridine diphosphate	UDP	$C_9H_{12}N_2O_8P_2$	404.17	Immediate precursor of polynucleotides. Precursor of uridine triphosphate
Uridine triphosphate	UTP	$C_9H_{12}N_2O_{10}P_3$	484.15	Precursor of uridine coenzymes (see Table pages 347-349)
Deoxythymidine monophosphate (thymidylic acid)	dTMP	$C_{10}H_{14}N_2O_7P$	322.21	Precursor of deoxythymidine diphosphate
Deoxythymidine diphosphate	dTDP	$C_{10}H_{14}N_2O_8P_2$	402.19	Precursor of deoxythymidine triphosphate
Deoxythymidine triphosphate	dTTP	$C_{10}H_{14}N_2O_{10}P_3$	482.17	Immediate precursor of deoxyribopolynuc
Deoxy-5-hydroxymethylcytidine monophosphate	dHMCMP	$C_{10}H_{16}N_4O_7P$	337.23	Constituent nucleotide of the deoxyribonu acid of T ₂ , T ₃ and T ₄ bacteriophages of <i>Esche</i> <i>ria</i> , in which it replaces deoxycytidine m phosphate
Deoxy-5-methylcytidine monophosphate	dMCMCP	$C_{11}H_{16}N_4O_7P$	321.23	Constituent of the deoxyribonucleic aci wheat germ, in which it partially replaces

Name	Formula and mol.wt.	Structure	Functions	Reference (see page 350)
Nicotinamide mononucleotide (NMN)	$C_{11}H_{15}N_2O_4P$ 334.22		Constituent of nicotinamide-adenine dinucleotide (NAD) and nicotinamide-adenine dinucleotide phosphate (NADP) (see below)	1
Nicotinamide-adenine dinucleotide (NAD) (diphosphopyridine nucleotide, DPN; coenzyme I; coenzyme I ₂ ; Co I; cozymase)	$C_{21}H_{27}N_7O_{14}P_2$ 663.44		Formed by the reaction: nicotinamide mononucleotide + ATP → NAD + pyrophosphate. Coenzyme of many dehydrogenases, in which function the pyridine ring of the molecule is reduced reversibly as follows: 	1
Nicotinamide-adenine dinucleotide phosphate (NADP) (triphosphopyridine nucleotide, TPN; coenzyme II; coenzyme II ₂ ; Co II; phospho-cozymase)	$C_{21}H_{27}N_7O_{17}P_3$ 743.42		Formed by the reaction: NAD + ATP → NADP + ADP. Coenzyme of many dehydrogenases, in which function the pyridine ring of the molecule is reduced reversibly as shown above	1

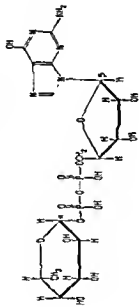
Table 12 (continued) Nucleotides with coenzyme functions

Name	Formula and mol. wt.	Structure	Functions	Reference (see page 350)
Acyl adenosine monophosphates (acyl-adenylates)	-	<p>where $R = \text{CH}_2 \cdot (\text{CH}_2)_n -$</p>	Formed by the reaction: fatty acid + ATP \rightarrow acyl adenosine monophosphate + pyrophosphate. Intermediate in activation of acetic acid and other fatty acids (page 391)	4
Aminoacyl adenosine monophosphates	-	<p>where $R = \text{amino-acid residue}$</p>	Intermediate in activation of amino acids for protein synthesis	5
Adenosine 5'-phospho-sulphate	$\text{C}_{10}\text{H}_{14}\text{N}_4\text{O}_{10}\text{P}_2\text{S}$ 427.29		Formed from ATP and inorganic sulphate. Intermediate in sulphate ester synthesis (see page 445)	6
Adenosine 3'-phospho 5'-phospho-sulphate	$\text{C}_{10}\text{H}_{14}\text{N}_4\text{O}_{11}\text{P}_3\text{S}$ 507.27		Formed from adenosine 5'-phosphosulphate and ATP. Donor of sulphate group in formation of esters of sulphuric acid (see page 445)	6

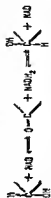
Probably intermediate in interconversions involving mannose.
Formed from mannose 1-phosphate and guanosine triphosphate



Naturally occurring precursor of L-fucose and form in which L-fucose is incorporated into milk oligosaccharides and probably other glycoproteins



Formed by the reaction: glucose 1-phosphate + UTP → uridine diphosphate + glucose + pyrophosphate. Precursor of uridine diphosphate glucosyl acid (see page 348). Intermediate in interconversion of glucose and galactose, uridine diphosphate glucose → uridine diphosphate galactose. In this reaction NAD is required for the consecutive oxidation and reduction of the 4-position of the hexose ring:



Intermediate in interconversion of galactose and glucose (see under "Uridine diphosphate glucose" above). Probable intermediate in formation of lactose

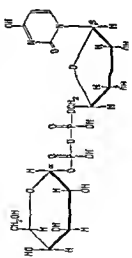
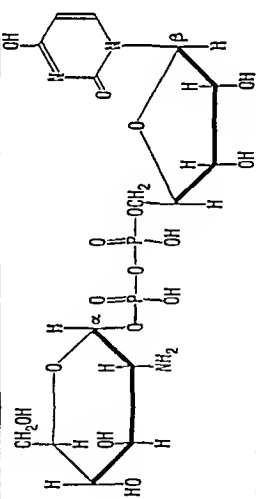
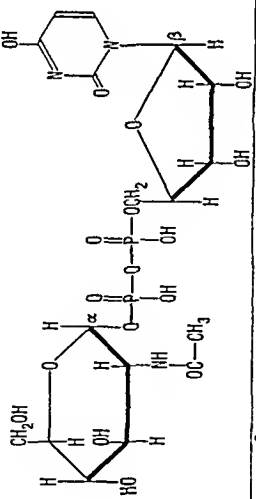
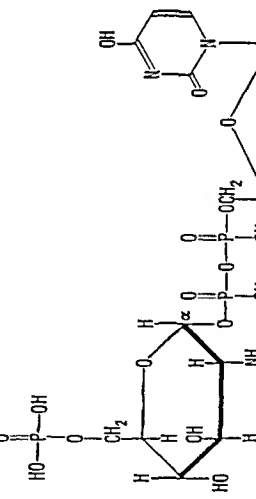
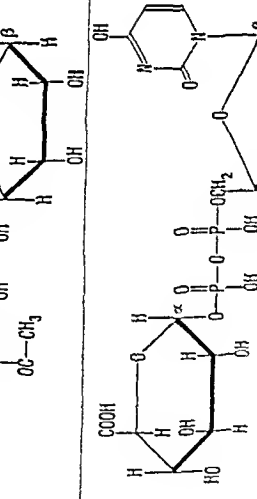
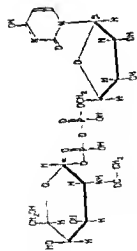


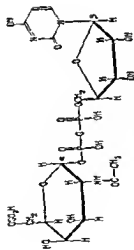
Table 12 (continued) Nucleotides with coenzyme functions

Name	Formula and mol.wt.	Structure	Functions	Reference (see page 350)
Uridine diphosphate glucosamine	$C_{18}H_{28}N_3O_{16}P_2$ 565.32		Intermediate in synthesis of mucopolysaccharides. Formed from uridine triphosphate and glucosamine 1-phosphate	10
Uridine diphosphate N-acetylglucosamine	$C_{19}H_{29}N_3O_{17}P_2$ 607.36		Intermediate in synthesis of mucopolysaccharides and glycoproteins	11
Uridine diphosphate acetylglucosaminic phosphate	$C_{19}H_{29}N_3O_{18}P_3$ 687.34		Intermediate in synthesis of mucopolysaccharides and glycoproteins	12
Uridine diphosphate glucuronic acid	$C_{18}H_{27}N_3O_{18}P_2$ 580.29		Formed from uridine diphosphate glucose by NAD-dependent oxidation. Donor of glucuronic acid in formation of glucuronide detoxication products, and probably also in formation of polysaccharides containing glucuronic acid (see page 423)	13



Uridine diphosphate
N acetyl
galactosamine

$C_{14}H_{19}N_5O_{11}P_2$
607.36



Uridine diphosphate
N acetyl
galactosamine
sulphate

$C_{14}H_{17}N_5O_{12}P_2S$
687.42



Cytidine diphosphate
glycerol

$C_{17}H_{24}N_4O_{11}P_2$
477.26



Cytidine diphosphate
ribitol

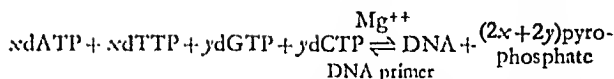
$C_{17}H_{24}N_4O_{11}P_2$
537.31

Table 12 (continued) Nucleotides with coenzyme functions

Name	Formula and mol. wt.	Structure	Functions	Reference
Cytidine diphosphate choline	$C_{44}H_{54}N_4O_{11}P_2$ 488.33		Formed from cytidine triphosphate and phosphorylcholine. Involved in formation of lecithin: cytidine diphosphate choline + α, β -diglyceride \rightarrow lecithin + cytidine monophosphate (see page 425)	17
Cytidine diphosphate ethanolamine	$C_{41}H_{50}N_4O_{11}P_2$ 446.25		Formed from cytidine triphosphate and phosphorylethanolamine. Involved in formation of cephalin (phosphatidylethanolamine) (see page 425)	17
Cytidine monophosphate N-acetylneuraminic acid	$C_{20}H_{27}N_3O_{10}P$ 614.46		Intermediate in incorporation of N-acetylneuraminic acid into milk oligosaccharides and other glycoproteins	18

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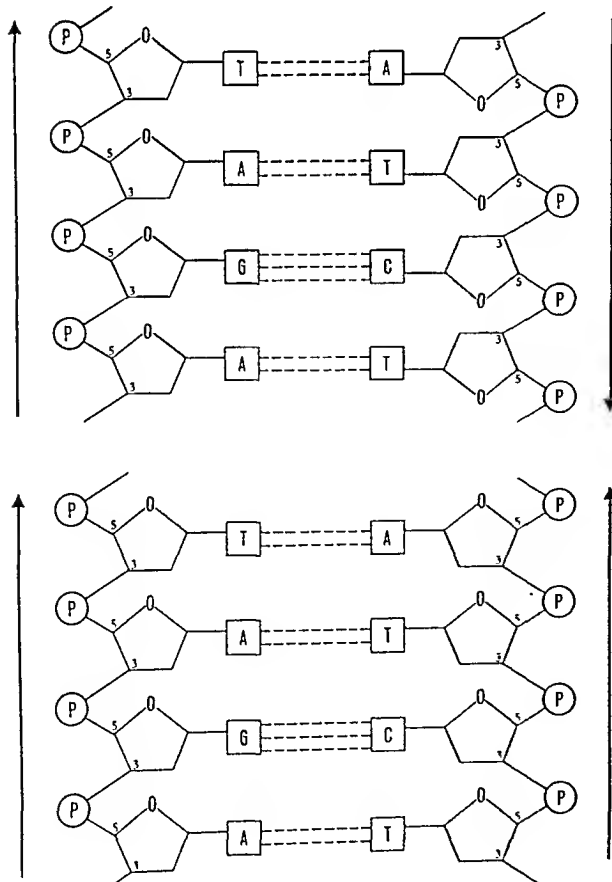


The enzyme has an absolute requirement for magnesium ions as well as for a 'primer' consisting of DNA. It requires all four deoxyribonucleotides if a primer containing all four deoxyribonucleotides is used. The enzyme is specific for the four deoxyribonucleoside triphosphates. Mono- and diphosphates are inactive, as are all ribonucleotides^{1,2}.

The base composition of the enzymatically formed DNA is a complementary copy of the base composition of the DNA used as primer, regardless of the relative amounts of each deoxyribonucleoside triphosphate added to the reaction mixture². This and other evidence⁴ shows that the enzymatic synthesis occurs by 'base-pairing' with the primer DNA. In other words, the role of the primer DNA is that of a DNA template. Where the DNA template contains the base adenine, the nucleotide inserted into the new molecule is the base thymine, and vice versa. Where the template contains the base guanine, the nucleotide inserted into the new molecule is cytosine, and vice versa². Such assembly can occur in two directions. In one direction the newly synthesized molecule of DNA has *opposite polarity* to the template molecule, i.e., the 3',5'-phosphodiester bridges in the template point in the opposite direction to the 3',5'-phosphodiester bridges of the newly synthesized molecule. In the other direction the newly synthesized molecule of DNA has *similar polarity*. Here the 3',5'-phosphodiester bridges of template DNA and newly formed DNA point in the same direction (Fig. 5). Experimental evidence shows that the newly synthesized DNA has the *opposite* polarity of the template. The product is double-stranded DNA. When the primer is double-stranded DNA it must presumably be 'unwound' into single-strand DNA before it can act as a

Fig. 5 Double-stranded DNA of opposite polarity (upper diagram) and of similar polarity (lower diagram). Experimental evidence shows that during the synthesis of DNA the new strand is of opposite polarity⁴

[A] Adenine; [T] Thymine; [G] Guanine; [C] Cytosine; [P] Phosphate



template for DNA synthesis. The mechanism for such 'unwinding' is not understood, but one possibility is that the 'unwinding' occurs just ahead of the growth of the new DNA chain⁵.

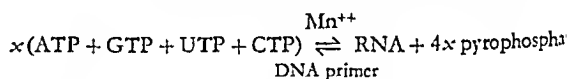
Using pure DNA polymerase, the total synthesis of infect viral DNA starting from the four deoxynucleoside triphosphates has been accomplished *in vitro*⁶.

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Synthesis of RNA

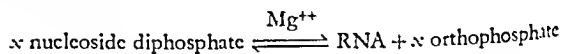
RNA nucleotidyltransferase (RNA polymerase). This enzyme catalyses the formation of RNA from nucleoside 5'-triphosphates¹:



The reaction requires all four ribonucleoside triphosphates and DNA primer. The product is RNA with a base composition that is a complementary copy of the DNA primer². The enzyme requires a bivalent metal ion, manganese being more effective than magnesium. The chief physiological function of this enzyme is probably to make messenger RNA for protein synthesis³, in other words, to transcribe information contained in the DNA code into RNA ('transcription'). This enzyme is also responsible for the synthesis of ribosomal RNA and s-RNA⁴. The nature of the RNA actually synthesized is determined by specific factors that adapt the enzyme to specific template DNA⁵.

Other types of RNA polymerases also exist. For example, viruses that contain RNA but not DNA can duplicate in host cells. In this case viral RNA acts as the template and DNA is not required for the *de novo* synthesis of RNA⁶.

Polyribonucleotide nucleotidyltransferase (polynucleotide phosphorylase). This enzyme catalyses the synthesis of polyribonucleotides from nucleoside 5'-diphosphates. The reverse reaction is termed phosphorolysis:



The RNA formed according to this equation will contain x mononucleotide units. The enzyme is specific for ribonucleoside diphosphates. Nucleoside mono- and triphosphates are inactive; also inactive are deoxyribonucleoside diphosphates⁷. The enzyme is relatively unspecific with respect to the base of the nucleoside diphosphate⁸. It can make polymers containing one or more bases. When the four ribonucleoside diphosphates containing adenine (A), guanine (G), cytosine (C), and uracil (U) are used, an RNA-like polymer results in which the base-sequence is random⁹. The synthesis of RNA shows a lag period that is abolished if an RNA primer is added^{10,11}. When a primer is supplied the enzyme adds new nucleotides to the ends of the primer molecules¹¹.

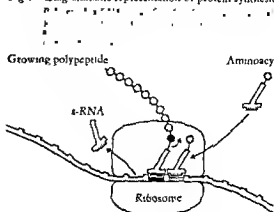
The function of this enzyme reaction is not yet understood. Its chief role may be not to synthesize but to degrade RNA. s-RNA is very resistant to phosphorolysis by polynucleotide phosphorylase, but the rapid breakdown of m-RNA may be catalysed by this enzyme⁸.

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Constituents of Living Matter – Nucleic Acids

Fig 6 Diagrammatic representation of protein synthesis:



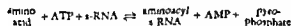
Synthesis of proteins 1-3

Protein synthesis involves the linking together of 20 different amino acids in specific sequences containing hundreds of amino acids. The amino-acid sequence of a particular protein is reproduced

into messenger RNA (m-RNA) by an enzyme, RNA polymerase, that requires DNA as a primer. This enzyme copies the base sequence of DNA into RNA. Each molecule of DNA is thus transcribed into two m-RNA molecules.

tural unit of protein synthesis, the ribosome

Amino acids are activated by attachment to another kind of RNA, namely soluble RNA (s RNA, transfer RNA)³ (see page 351).

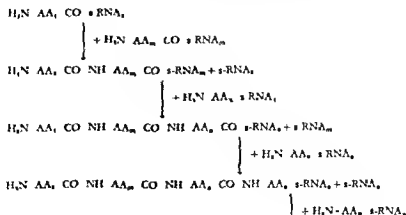


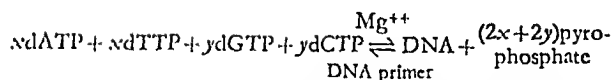
The reaction proceeds through the intermediate formation of aminoacyl AMP. For each amino acid there are at least one specific activating enzyme and one specific type of t-RNA. Each amino-

and aminoacyl s-RNA are brought together. This can be p
as shown in Figure 6 above.

In Figure 6 the divisions along the m-RNA are intended to represent coding information equivalent to one amino acid. One new aminoacyl-t-RNA can fit into the ribosomal frame. The specific kind of aminoacyl-t-RNA is determined by the sequence of the m-RNA.

reaches the end of the newly synthesized protein molecule the s-RNA must be lost by hydrolysis, but the details of the release of the protein molecule from the ribosome are not clear at present. UAA, UAG and UGA are thought to be the triplets that terminate polypeptide synthesis.¹²





The enzyme has an absolute requirement for magnesium ions as well as for a 'primer' consisting of DNA. It requires all four deoxyribonucleotides if a primer containing all four deoxyribonucleotides is used. The enzyme is specific for the four deoxyribonucleoside triphosphates. Mono- and diphosphates are inactive, as are all ribonucleotides^{1,2}.

The base composition of the enzymatically formed DNA is a complementary copy of the base composition of the DNA used as primer, regardless of the relative amounts of each deoxyribonucleoside triphosphate added to the reaction mixture³. This and other evidence⁴ shows that the enzymatic synthesis occurs by 'base-pairing' with the primer DNA. In other words, the role of the primer DNA is that of a DNA template. Where the DNA template contains the base adenine, the nucleotide inserted into the new molecule is the base thymine, and vice versa. Where the template contains the base guanine, the nucleotide inserted into the new molecule is cytosine, and vice versa². Such assembly can occur in two directions. In one direction the newly synthesized molecule of DNA has *opposite polarity* to the template molecule, i.e., the 3',5'-phosphodiester bridges in the template point in the opposite direction to the 3',5'-phosphodiester bridges of the newly synthesized molecule. In the other direction the newly synthesized molecule of DNA has *similar polarity*. Here the 3',5'-phosphodiester bridges of template DNA and newly formed DNA point in the same direction (Fig. 5). Experimental evidence shows that the newly synthesized DNA has the *opposite* polarity of the template. The product is double-stranded DNA. When the primer is double-stranded DNA it must presumably be 'unwound' into single-strand DNA before it can act as a

template for DNA synthesis. The mechanism for such 'unwinding' is not understood, but one possibility is that the 'unwinding' occurs just ahead of the growth of the new DNA chain⁵.

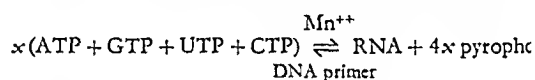
Using pure DNA polymerase, the total synthesis of a viral DNA starting from the four deoxynucleoside triphosphates has been accomplished *in vitro*⁶.

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Synthesis of RNA

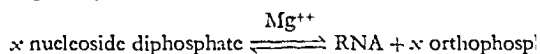
RNA nucleotidyltransferase (RNA polymerase). This enzyme catalyses the formation of RNA from nucleoside 5'-triphosphates.



The reaction requires all four ribonucleoside triphosphates as primer. The product is RNA with a base composition which is a complementary copy of the DNA primer². The enzyme requires a bivalent metal ion, manganese being more effective than magnesium. The chief physiological function of this enzyme is probably to make messenger RNA for protein synthesis³, i.e., to transcribe information contained in the DNA code (transcription). This enzyme is also responsible for the synthesis of ribosomal RNA and 5-RNA⁴. The nature of the actually synthesized RNA is determined by specific factors that act on the enzyme to specific template DNA⁵.

Other types of RNA polymerases also exist. For example, some viruses contain RNA but not DNA can duplicate in host cells. In this case viral RNA acts as the template and DNA is not required for the *de novo* synthesis of RNA⁶.

Polyribonucleotide nucleotidyltransferase (polynucleotide phosphorylase). This enzyme catalyses the synthesis of polyribonucleotides from nucleoside 5'-diphosphates. The reverse reaction is the phosphorolysis:



The RNA formed according to this equation will contain x nucleotide units. The enzyme is specific for ribonucleoside diphosphates. Nucleoside mono- and triphosphates are inactive; all active are deoxyribonucleoside diphosphates⁷. The enzyme is relatively unspecific with respect to the base of the nucleoside diphosphate⁸. It can make polymers containing one or more bases. When the four ribonucleoside diphosphates containing adenine, guanine (G), cytosine (C), and uracil (U) are used, an RNA polymer results in which the base-sequence is random⁹. The synthesis of RNA shows a lag period that is abolished if an RNA primer is added^{10,11}. When a primer is supplied the enzyme new nucleotides to the ends of the primer molecules¹¹.

The function of this enzyme reaction is not yet understood. Its chief role may be not to synthesize but to degrade RNA. s-RNA is very resistant to phosphorolysis by polynucleotide phosphorylase but the rapid breakdown of m-RNA may be catalysed by this enzyme⁸.

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Fig. 5 Double-stranded DNA of opposite polarity (upper diagram) and of similar polarity (lower diagram). Experimental evidence shows that during the synthesis of DNA the new strand is of opposite polarity⁴.

[A] Adenine; [T] Thymine; [G] Guanine; [C] Cytosine; [P] Phosphate

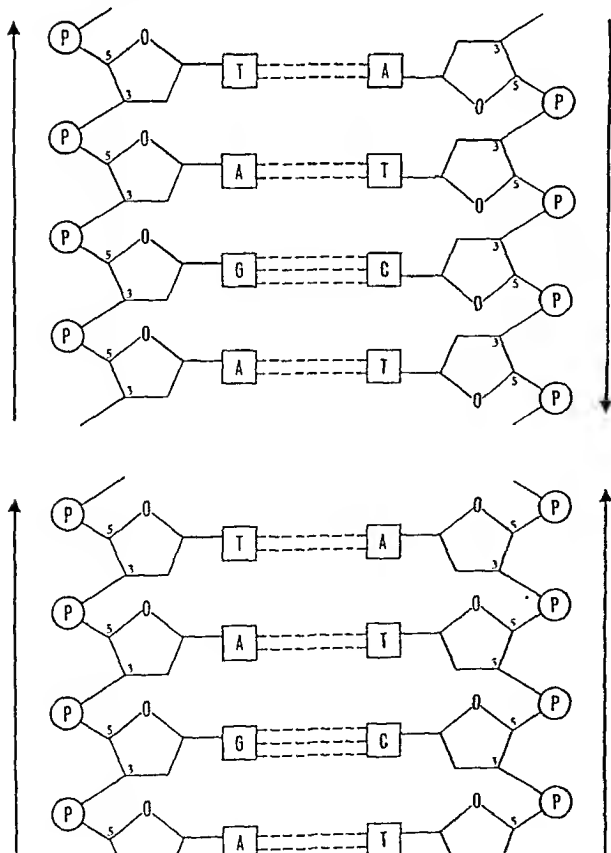
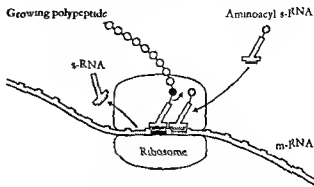


Fig 6 Diagrammatic representation of protein synthesis

Polypeptide s-RNA is transferred to the new aminoacyl s-RNA. The growing polypeptide s-RNA together with the m-RNA then moves along the ribosome from right to left by one division. A molecule of s-RNA is released.



The scheme shows that proteins grow by the stepwise addition

heals of proteins 1-3

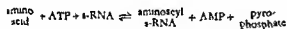
rotein synthesis involves the linking together of 20 different acids in specific sequences containing hundreds of amino acids. The amino-acid sequence of a particular protein is reproduced over and over again in each protein molecule synthesized. The amino-acid sequence is exceedingly rare. The exact

RNA (an 'anticodon' or 'codon')¹⁰ In bacteria, protein chains (codons AUG, GUG) have been shown to be initiated by formyl-methionyl-s-RNA.

The assembly of the polypeptide occurs on the ribosome. The function of the ribosome is that of a framework on which m-RNA and aminoacyl-s-RNA are brought together. This can be pictured as shown in Figure 6 above.

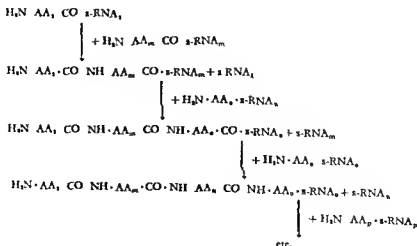
In Figure 6 the divisions along the m-RNA are intended to

Amino acids are activated by attachment to another kind of RNA, namely soluble RNA (s-RNA, transfer-RNA)¹⁰ (see page 351).



The reaction proceeds through the intermediate formation of aminoacyl AMP. For each amino acid there are at least one specific activating enzyme and one specific type of s-RNA. Each amino acid activating enzyme thus recognizes one specific

liberated and dissociates from the ribosome. This process requires transfer enzymes¹¹⁻¹³. The m-RNA and polypeptide s-RNA must now move along the ribosomal framework by one segment, and the process is then repeated. When the synthetic mechanism reaches the end of the newly synthesized protein molecule the last



The transfer of amino acid from aminoacyl-s-RNA to ribosomal polypeptide requires GTP^{11,12}. The role of GTP in this reaction is not understood.

Electron microscopy reveals that ribosomes actively engaged in protein synthesis appear like beads strung on a thread¹⁴. It has also been shown that ribosomes active in protein synthesis have a much higher molecular weight than those not active¹⁵. This evidence has been interpreted to show that more than one ribosome can be attached to each molecule of m-RNA. The assembly of one molecule of protein starts before the assembly of another, further along the molecule of m-RNA, has been completed.

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Minor (infrequently occurring) constituents of nucleic acids

More than 20 minor purine and pyrimidine nucleosides have been found in hydrolysates of RNA isolated from various organisms. There are several classes of these minor components. In the largest class the bases are methylated. The majority of the theoretically possible methylated derivatives of the common bases have been found. Another class has the sugar linked to an unusual position of the base. Yet another class has a hydroxyl group of the sugar methylated. Of these minor constituents 18 have been isolated from a single source, namely s-RNA from yeast¹.

The minor constituents arise by direct methylation of the RNA molecule, and the enzymes responsible are referred to as RNA methylases. At least 8 separate RNA methylases have been demonstrated. These enzymes are widely distributed in living organisms². The methylated bases are not distributed at random but are specifically located in the RNA molecule. The biological significance of the methylated bases is not known, but it has been suggested that they constitute part of the recognition mechanism in the transfer of genetic information².

Several minor components have also been found in addition to the four common bases of DNA. The DNA of animals and plants contains 5-methylcytosine³ and that of certain bacteria contains 6-methyladenosine⁴. These constituents arise by direct methylation of DNA. At least two DNA methylases exist. One methylates adenine and the other cytosine of DNA².


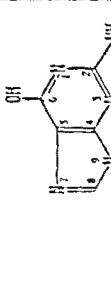


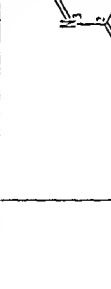
A summary of these minor nucleosides of the nucleic acids is given in Table 13⁵.

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Table 13 Minor (infrequently occurring) nucleosides found in nucleic acids

The minor nucleosides are listed below the formula of the parent compound. Although shown as a parent compound, inosine is itself one of the minor nucleosides.

Adenosine	Guanosine	Inosine	Cytidine	Uridine
				
N ⁴ -Methyladenosine N ⁶ ,N ⁶ -Dimethyladenosine 2-Methyladenosine 2'-O-Methyladenosine	1-Methylguanosine 7-Methylguanosine N ⁷ -Methylguanosine N ² ,N ² -Dimethylguanosine 2'-O-Methylguanosine N ⁷ -Ribosylguanine	1-Methylinosine	3-Methylcytidine 5-Methylcytidine 2'-O-Methylcytidine	3-Methyluridine 5-Methyluridine* 2'-O-Methyluridine Pseudouridine** 2'-O-Methylpseudouridine**

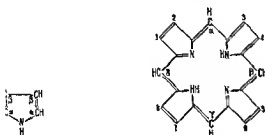
* This compound is the ribose-containing analogue of thymidine. ** Pseudouridine is 5-ribosyluracil.

(For references see page 363)

ysins^{1,2}

hryns are tetrapyrrolic pigments sometimes found free in but more commonly occurring as divalent metal-ion com- usually conjugated with proteins. Such proteins often func- i enzymes.

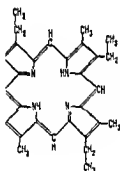
parent compound of the porphyrins is *porphyr*, in the mole- which one pyrrole ring and 3 pyrrole-like rings are linked er through their α -carbon atoms by means of methene (-) bridges



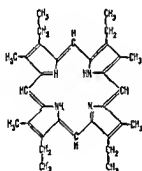
Pyrrole

Porphyrin

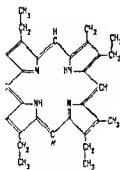
e porphyrin molecule thus forms a closed ring of carbon and ten atoms lying in one plane and containing a central 16-mem- ring of 12 carbon and 4 nitrogen atoms



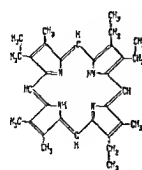
I



II

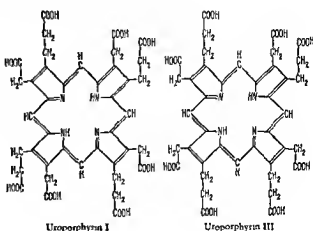


III



IV

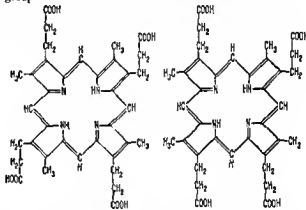
these isomers, known as types I-IV porphyrins, provide the basis for the classification of the naturally occurring porphyrins



Uroporphyrin I

Uroporphyrin III

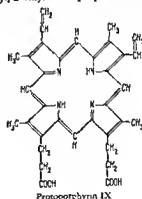
Decarboxylation of the 4 acetic acid groups gives rise to the *coproporphyrins*, which contain 4 methyl and 4 propionic acid groups



Coproporphyrin I

Coproporphyrin III

Decarboxylation and dehydrogenation of two of the propionic acid groups of coproporphyrin III yield *protoporphyrin IX*, which contains 4 methyl, 2 vinyl and 2 propionic acid groups

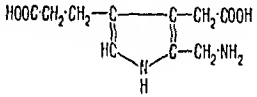
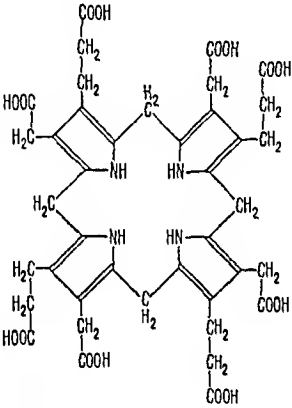
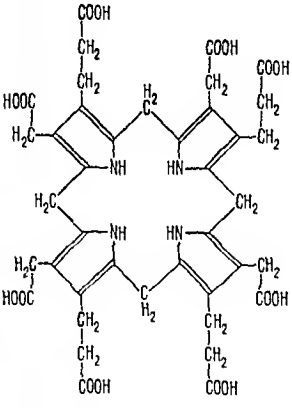
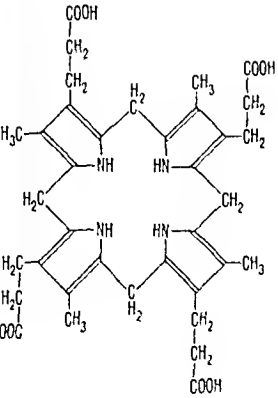


Protoporphyrin IX

[PAPER 309-311]

Data on the naturally occurring porphyrins are summarized in Table 14 on pages 356-359. On the biosynthesis of porphyrins see page 436, on the porphyrins see pages 454-455.

Table 14 Porphyrins of biological importance (and their precursors)

Porphyrin	Structure	Occurrence
<p>Prophobilinogen $C_{10}H_{14}N_4O_4$</p>		<p>Obligatory precursor for the biosynthesis of porphyrins and haem. Present in urine in hepatic porphyria, and in poisoning by lead and monoureide sedatives</p>
<p>Uroporphyrinogen I $C_{40}H_{44}N_4O_{16}$</p>		<p>Metabolite of prophobilinogen</p>
<p>Uroporphyrinogen III $C_{40}H_{44}N_4O_{16}$</p>		<p>Metabolite of prophobilinogen</p>
<p>Coproporphyrinogen I $C_{38}H_{44}N_4O_8$</p>		<p>Metabolite of prophobilinogen</p>

(continued) Porphyrins of biological importance (and their precursors)

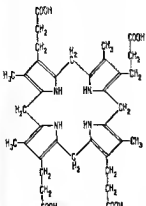
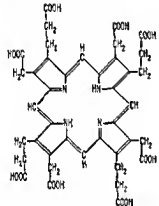
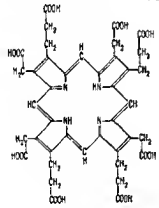
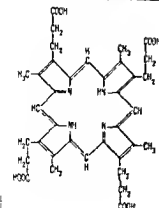
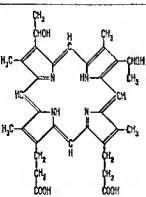
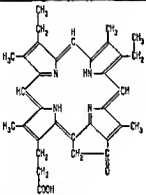
Porphyrin	Structure	Occurrence
prophorphytanogen III $C_{44}H_{60}N_4O_8$		Metabolite of porphobilinogen
porphyrin I $C_{44}H_{60}N_4O_8$		Found in large amounts in erythrocytes and other tissues, especially the teeth and bones of patients with erythropoietic porphyria. Also present in small amounts in urine
prophosphin III $C_{44}H_{60}N_4O_8$		Found in very small amounts in human urine, in larger amounts in some forms of porphyria and lead poisoning
proprophyrin I $C_{44}H_{60}N_4O_8$		Found in large amounts in erythrocytes and other tissues, especially the teeth and bones of patients with erythropoietic porphyria. Also present in small amounts in urine

Table 14 (continued) Porphyrins of biological importance

Porphyrin	Structure	Occurrence
Coproporphyrin III $C_{31}H_{34}N_4O_4$		Found free in faeces, urine, erythrocytes, bile, yeast and bacteria. Increased pathologically in porphyria and porphyria. Also formed in the putrefaction of meat
Protoporphyrin IX $C_{31}H_{34}N_4O_4$		Found in bone marrow, erythrocytes, liver and faeces. The iron complexes form the prosthetic groups of haemoglobin, myoglobin, catalase, peroxidases and cytochrome b. Also formed in the putrefaction of meat
Mesoporphyrin IX $C_{31}H_{34}N_4O_4$		Occurs in normal human faeces, possibly also in human fistula bile
Deuteroporphyrin IX $C_{30}H_{30}N_4O_4$		Occurs in human faeces after ingestion of blood or following haemorrhages of the gastro-intestinal tract. Formed together with protoporphyrin and coproporphyrin in the putrefaction of meat

(For references see page 363)

ded) Porphyrins of biological importance

thyrin	Structure	Occurrence
Protophyrin IX O_4		Probably not of biological importance. Natural occurrence not definitely established, but may be present in natural coproporphyrin and deuteroporphyrin fractions
Uroporphyrin O_4		Occurs in large amounts in bile and faeces of ruminants. Causes photosensitization if bile flow is impeded

omenclature of iron porphyrins

Coordination position occupied by		LEWIS and LEWIS ¹	Authors	
(a)	(b)		PAULING ² , BARON ³	ANSON ⁴ , KEILIN ⁵
H ₂ O	H ₂ O	Heme*	Ferroheme	Haem
OH	H ₂ O	Hematin**	Ferrheme hydroxide	Haematin
Cl	-	Hemin	Ferrheme chloride	Haemin
N-Compound	N-Compound	Hemochrome	Ferro-hemochromogen	Haemochromogen
N-Compound	N-Compound	Hemochrome	Ferr-hemochromogen	Para-haematin
Globin	H ₂ O	Hemoglobin	Hemoglobin	Haemoglobin
Globin	O ₂	Oxyhemoglobin	Oxyhemoglobin	Oxyhaemoglobin
Globin	H ₂ O	Hemoglobin	Ferrhemoglobin	Acid methaemoglobin
Globin	OH	Hemoglobin hydroxide	Ferrhemoglobin hydroxide	Alkaline methaemoglobin
Globin	CO	Carboxyhemoglobin	Carbon monoxide hemoglobin	-

ferred to by some authors as ferroporphyrin ** Also referred to by some authors as ferroporphyrin hydroxide

ins (haem derivatives)

ncy of porphyrins to form complexes with divalent

iron atom can be occupied by various molecules or groups (a and b in Table 15). The term haem itself is used to designate the complex of protoporphyrin IX with ferrous iron (Fe⁺⁺), where the two coordination positions are occupied by water molecules.

Constituents of Living Matter – Porphyrins

(For references see page 363)

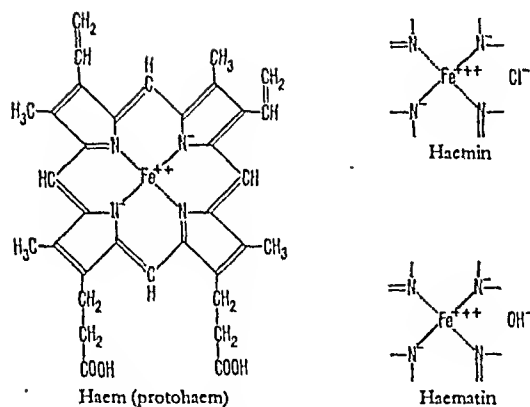
b/e 16 Iron porphyrins and haem proteins of biological importance

Substance	General nature	Spectral characteristics		Remarks
		Solvent	Absorption maxima in nm	
aem (protohaem) $C_{34}H_{32}N_4O_4Fe$	Ferrous iron complex of protoporphyrin IX. Extremely unstable. Easily oxidized to haematin. See also pages 359 and 362	Phosphate buffer pH7.0	575 550 415	Prosthetic group of haemoglobin. Combines with many nitrogenous bases to form haemochromes
aematin $C_{34}H_{30}N_4O_4Fe$ (OH)	Ferric iron complex of protoporphyrin IX. Moderately stable. See also pages 359 and 362	Acetic acid 10% NaOH Ether	630–635 540 510 400 580 650	Formed from haemoglobin in blood under many different conditions. The pigment of the malarial parasite <i>Plasmodium</i> has been shown to consist of haematin ⁸
haemoglobin (Hb) (deoxyhaemoglobin)	Compound of globin with 4 molecules of haem. Iron is in the ferrous state and readily oxidized. Globin portion consists of 4 polypeptide chains in the form of 2 pairs of identical chains. The great variety of abnormal haemoglobins is accounted for by differences in the amino-acid sequence and in the way the chains are combined ⁹ (see also pages 446–448). On the spatial arrangement of the haemoglobin molecule see the literature ¹⁰	Water	560 430	Oxygen carrier in erythrocytes of all vertebrates. One erythrocyte contains ca. 280 million Hb molecules. Combines reversibly with oxygen to form oxyhaemoglobin, and with carbon monoxide to form carboxyhaemoglobin (affinity for carbon monoxide over 100 times that for oxygen)
myoglobin (myohaemoglobin, deoxymyoglobin)	Unlike haemoglobin, consists of one haem molecule combined with a polypeptide of 153 amino-acid residues ⁹ . Iron is in the ferrous state. On the spatial arrangement of the myoglobin molecule see the literature ¹⁰	Water	555 435	Found in muscles of higher vertebrates, nematodes and molluscs, where its main function is oxygen storage. Completely saturated with oxygen at low pressures. The affinity of myoglobin for oxygen is greater than that of haemoglobin
oxyhaemoglobin	Compound of haemoglobin with 4 molecules of oxygen available physiologically. Iron is in the ferrous state	Water	577 540 412	Present in fresh blood of all vertebrates (see also under 'Haemoglobin' above)
carboxyhaemoglobin	Compound of 4 molecules of carbon monoxide with the 4 iron atoms of haemoglobin	Water	568–572 538 418	Rapidly formed in the body during exposure to carbon monoxide, resulting in failure of oxygen transport by haemoglobin (see also under 'Haemoglobin' above)
methaemoglobin (methaemoglobin)	Similar to haemoglobin except that iron is in the ferric state	Acid solution Alkaline solution	630 500 405 577 540 411	Formed reversibly from haemoglobin by oxidation (ferricyanide, nitrites, chlorates, etc.). Occurs in erythrocytes in larger amounts in some pathological conditions ¹⁰
hologlobin (verdoglobin A, verdohaemoglobin)	Haemoglobin-like compound in which the α -methene bridge is oxidized; formed by coupled oxidation of haemoglobin	Water	670 630	Possibly a normal haemoglobin degradation product and intermediary in bile pigment formation

(For references see page 363)

6 (continued) Iron porphyrins and haem proteins of biological importance

Substance	General nature	Spectral characteristics		Remarks
		Solvent	Absorption maxima in cm	
haemoglobin (deoxyhaemoglobin S)	Chemical structure not known	Water	620	Formed irreversibly from haemoglobin by action of hydrogen sulphide. Present in erythrocytes after ingestion of sulphur, sulphonanilides, aromatic amines, occasionally trinitrotoluene, also in septicæmia (especially <i>Clostridium perfringens</i> bacteraemia) and severe constipation.
Cytochrome a group: a, a ₁	Prosthetic group is a haem containing a formyl side chain	Water	(Ferro-ferri difference spectrum) Cytochrome a: 605 (α) 444 (γ) Cytochrome a ₁ : 605 (α) 445 (γ)	Cytochromes a and a ₁ are components of the cytochrome c oxidase of the mitochondria of animals, plants and yeast ²⁰ . Ferrocycytochrome a ₁ combines with cyanide and carbon monoxide, whereas ferrocycytochrome a does not. The cyanide compound of ferrocycytochrome a ₁ is autooxidizable. Cytochromes a and a ₁ may be part of the same protein ('cytochrome aa').
Cytochrome c group: c, c ₁	Possess covalent linkages between haem side chains and protein. Only thioether linkages are so far known, and the prosthetic groups can be called 'substituted mesohaems'.	Water	Ferrocycytochrome c: 550 (α) 520 (β) 415 (γ) Ferrocycytochrome c ₁ : 553 (α)	Cytochromes c and c ₁ are found in the mitochondria of animals, plants and yeast. At neutral pH the former is relatively heat-stable, the latter not. Cytochrome c has an isoelectric point above pH 7 and the oxidation of its ferro form by oxygen is catalysed by cytochrome oxidase; the oxidation-reduction potential over most of the physiological pH range is ca + 0.25 V.
Cytochrome b group: b, b ₁	Prosthetic group is protohaem	Water	Ferrocycytochrome b: 564 (α) Ferrocycytochrome b ₁ : 556 (α)	Cytochrome b occurs in the mitochondria of animals, plants and yeast. Cytochrome b ₁ is found in animal microsomes. It is reduced by NADH in the presence of cytochrome b ₁ reductase.
Cytochrome d group: d (a ₁)	Prosthetic group is an iron-dihydroporphyrin (phytylchlorin) complex	Water	Ferrocycytochrome d: 645	Found in some bacteria (e.g., <i>E. coli</i> , <i>Aerobacter peroxidans</i>). The ferro form is autooxidizable and combines with carbon monoxide.
Oxidases	Prosthetic group is haematin or a related compound	Weak acids	645 583 548 498 (horse-radish peroxidase)	Occur in plants and animals. Biological functions not well known.
Catalase	Prosthetic group is haematin	Water	629 544 506 409 280	Decomposes hydrogen peroxide. Present in respiring cells, highly active in liver, erythrocytes, etc. Catalytic activity inhibited by cyanide, hydrogen sulphide, hydroxylamine, azides, aminophenols and 2,4-dinitrophenol.



Haem and other ferrous complexes of the porphyrins readily react with bases such as primary amines, pyridine, ammonia, imidazole compounds (e.g., histidine) and hydrazine, the resulting products being known as *haemochromes*.

Haemoproteins are conjugated proteins in which the prosthetic group is haem. They are of two types: 'haemochromes', in which the two free coordination bonds of the haem iron atom are occupied by nitrogen atoms of basic side chains of the protein, and 'open' type haemoproteins, in which at least one of these bonds is not so occupied. Haemoglobin and myoglobin are haemoproteins of the open type, as are catalases and peroxidases, though in the latter the nature of the iron-coordinating groups is not known for certain.

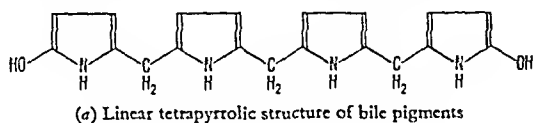
Three types of physiologically active haemoproteins, depending on the valency state of the iron, can be distinguished:

1. Fe remains divalent: haemoglobin, myoglobin
2. Fe is reversibly oxidized and reduced: cytochromes
3. Fe remains trivalent: catalase and peroxidases

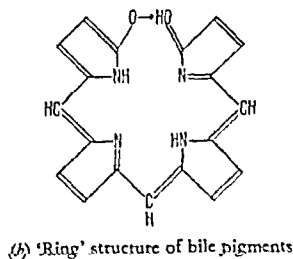
Haemoglobin is the principal representative of a class of haemoproteins whose function is to combine reversibly with oxygen; this reaction does not involve rapid oxidation of the haem iron atom. *Catalases* and *peroxidases* are enzymes responsible for catalysis of electron and/or hydrogen transport, the hydrogen acceptor being either hydrogen peroxide or one of its alkyl derivatives. *Cytochromes* are by definition haemoproteins whose characteristic function is also electron and/or hydrogen transport, but by means of a reversible valency change in their haem iron atom (ferrocyclochrome \rightleftharpoons ferricyclocchrome). For further data on haemoproteins see Table 16, pages 360–361.

Bile pigments^{1,11}

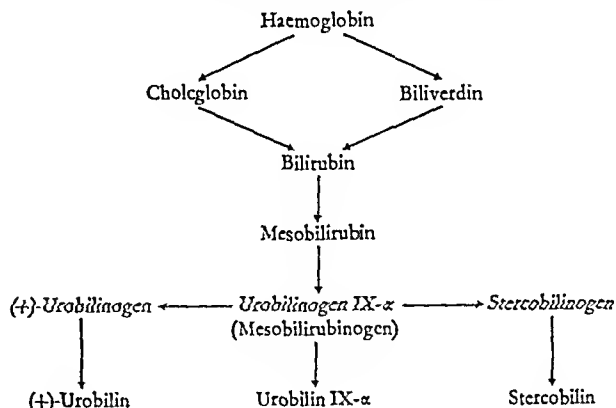
The metabolic breakdown of the haemoglobin released by the disintegration of erythrocytes results in the formation of bile pigments. The breakdown occurs by the oxidative cleavage of the porphyrin ring with the loss of a carbon atom to form open-chain tetrapyrroles. Bile pigments are generally represented as linear tetrapyrrolic chains with terminal hydroxyl groups:



but their structure is more correctly represented by a tetrapyrrolic 'ring', closed by a hydrogen bond between oxygen atoms:



protoporphyrin is released from the globin, with choleglobin as intermediate¹². The iron released by the catabolism of haemoglobin is largely retained in the body in the form of the protein ferritin, while the bile pigments are excreted. Current views about the formation in the organism of the various bile pigments (see also Table 17, pages 363–364) can be summarized as follows¹³:



The principal sites of conversion of the haem portion of haemoglobin to bilirubin are believed to be the reticuloendothelial cells of the liver, spleen and bone marrow. In the blood, bilirubin becomes bound to serum albumin (see also pages 576–577) and is rapidly taken up by the liver, whence it reaches the intestine via the bile. The further degradation takes place mainly in the intestine.

VAN DEN BERGH and MÜLLER¹⁴ were the first to observe that there is a difference between serum bilirubin and the bilirubin-like pigments excreted in bile in respect of their coupling with diazotized sulphanilic acid, the latter pigments reacting directly whereas serum bilirubin requires the presence of ethanol (direct and indirect VAN DEN BERGH reactions respectively). Subsequently it was shown¹⁵ that bilirubin undergoes conjugation in the liver cells with glucuronic acid (and possibly other substances) and is excreted into the bile mainly as the diglucuronide and to a smaller extent as the monoglucuronide. This conjugated bilirubin is water-soluble, whereas bilirubin itself is soluble in lipids but insoluble in water. This difference in solubility explains not only the difference in the VAN DEN BERGH reaction but also that in the physiological behaviour of the two types of pigment. Thus it accounts for the fact that bile pigments are excreted in the urine in obstructive jaundice and hepatitis but not in haemolytic jaundice (see below). Since lipids have an affinity for brain tissue, it also explains why a great excess of bilirubin in the blood of infants results in kernicterus.

Jaundice

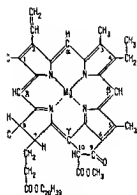
Jaundice may broadly be classified into the haemolytic, obstructive and hepatogenous varieties. In haemolytic jaundice the excessive rate of breakdown of erythrocyte haemoglobin causes bilirubin to pass into the blood stream at a rate greater than that at which it can be conjugated and removed by the liver. Obstructive jaundice occurs when there is obstruction to the outflow of bile from the liver through the biliary ducts. In hepatogenous jaundice destruction of the normal architecture of the liver causes bile pigment to enter the blood stream. In both the latter cases the water-soluble bile pigment is excreted in the urine. See also pages 576–577.

Bilirubinoids

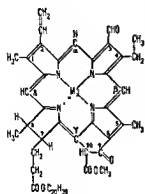
The various intermediates (bilirubinoids) in the conversion of bilirubin to stercobilin by the reductive enzymes of the intestinal bacteria may be partly reabsorbed in the intestinal tract and either returned to the liver or excreted in the urine. Data on the most important of these compounds are summarized in Table 17, pages 363 and 364.

Chlorophylls

Other metallo-porphyrins occurring in nature include the magnesium porphyrin compounds that are components of the chlorophyll of green plants. The latter has been shown to consist mainly of a mixture of chlorophyll a and chlorophyll b, both of which contain a porphyrin esterified with the long-chain optically active *faty* alcohol *phytyl* and magnesium. The porphyrins are charac-



Chlorophyll a



Chlorophyll b

and d. In leaf tissue, chlorophylls exist in the form of a protein

References

¹ For reviews see LEVING and LEGGE, *Hematin Compounds and Bile Pigments*, Interscience, New York, 1949

¹³ (1948)

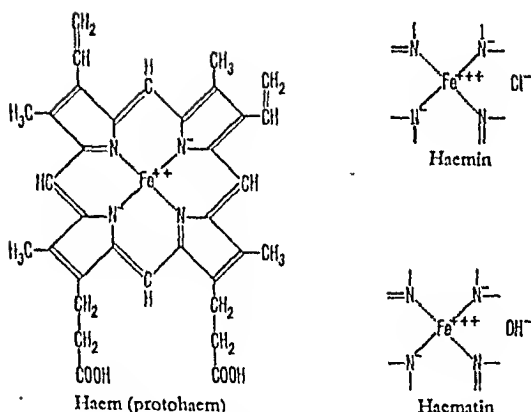
¹⁴ GRAY, C.H., *The Bile Pigments*, Methuen, London, 1953; GRAY, C.H., *Bile Pigments in Health and Disease*, Thomas, Springfield, Ill., 1961; WITTH, T.K., *Bile Pigments*, Academic Press, New York, 1968; SCHWITZ, R., in STANBURY et al. (eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966

Cyanocobalamin (vitamin B₁₂)

the soluble fraction of liver ex-

Table 17 Bilirubinoids and related compounds

Substance	Structure	Remarks
Bilirubin $C_{57}H_{72}N_4O_6$		Breakdown product of haemoglobin and other haem compounds in reticuloendothelial system. Present in excess in serum and tissues in haemolytic jaundice. Also found in urine and faeces of infants. Conjugated in liver cells with glucuronic acid to form bile pigment.
Biliverdin $C_{54}H_{64}N_4O_6$		Breakdown product of haemoglobin, reduced enzymatically in liver to bilirubin. Not found in urine or faeces of normal adults.
Mesobilirubin $C_{55}H_{70}N_4O_6$		May be present in the small intestine as reduction product of bilirubin.
Mesobilane (mesobilirubinogen, urobilinogen IX-α) $C_{55}H_{72}N_4O_5$		Degradation product of bilirubin in liver. Present in normal bile, urine and faeces; increased in pathological conditions.



Haem and other ferrous complexes of the porphyrins readily react with bases such as primary amines, pyridine, ammonia, imidazole compounds (e.g., histidine) and hydrazine, the resulting products being known as *haemochromes*.

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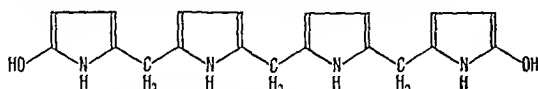
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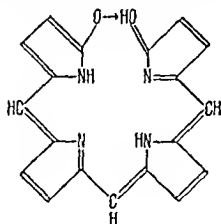
Bile pigments^{1,11}

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(a) Linear tetrapyrrolic structure of bile pigments

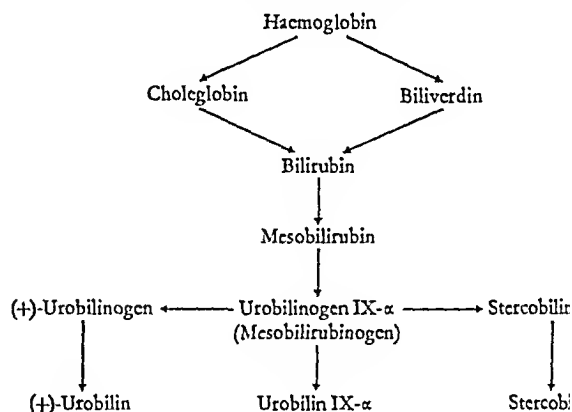
but their structure is more correctly represented by a tetrapyrrolic 'ring', closed by a hydrogen bond between oxygen atoms:



(b) 'Ring' structure of bile pigments

All naturally occurring bile pigments are derived from protoporphyrin IX by fission at the α -methene link. The possibility exists that the oxidative cleavage of the porphyrin ring occurs before the

protoporphyrin is released from the globin, with choleglo intermediate¹². The iron released by the catabolism of haemoglobin is largely retained in the body in the form of the protein tin, while the bile pigments are excreted. Current views also formation in the organism of the various bile pigments (see Table 17, pages 363–364) can be summarized as follows¹³:



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Jaundice

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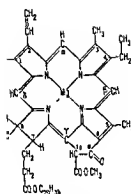
Bilirubinoids

The various intermediates (bilirubinoids) in the conversion of bilirubin to stercobilin by the reductive enzymes of the intestine: bacteria may be partly reabsorbed in the intestinal tract and either returned to the liver or excreted in the urine. Data on the most important of these compounds are summarized in Table 17, pages 363 and 364.

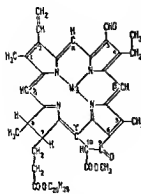
Chlorophylls

Other metallo-porphyrins occurring in nature include the magnesium porphyrin compounds that are components of the chlorophyll of green plants. The latter has been shown to consist mainly of a mixture of chlorophyll a and chlorophyll b, both of which contain a porphyrin esterified with the long-chain optically active fatty alcohol phytol and magnesium. The porphyrins are characterized by the presence of an additional isocyclic ring.

Phytol is also a component of vitamin K₁ (see page 468). Spectral data have indicated the existence of two further chlorophylls,



Chlorophyll a



Chlorophyll b

References

- ¹ For reviews see LAMBEAG and LEGGE, *Haematin Compounds and Bile Pigments*, 1961.
- ² GRAY, C.H., *The Bile Pigments*, Methuen, London, 1953; GRAY, C.H., *Bile Pigments in Health and Disease*, Thomas, Springfield, Ill., 1961; WIRTH, T., *Bile Pigments*, Academic Press, New York, 1968; SCHMID, R., in STAMM et al. (Eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966.

and d. In leaf tissue, chlorophylls exist in the form of a protein complex, chloroplastin, which has been isolated.¹⁴

The photosynthetic purple sulphur bacteria contain the pigment bacteriochlorophyll. This has been shown to differ from chlorophyll a only in the presence of an acetyl group in place of the vinyl group in position 2 and in the hydrogenation of the 3,4 double bond.

Cyanocobalamin (vitamin B₁₂)

Cyanocobalamin, the cobalt-containing principle of liver ex-

Table 17 Bilirubinoids and related compounds

Substance	Structure	Remarks
Bilirubin $C_{43}H_{56}N_4O_6$		Breakdown product of haemoglobin and other haem compounds in reticuloendothelial system. Present in excess in serum and tissues in haemolytic jaundice. Also found in urine and faeces of infants. Conjugated in liver cells with glucuronic acid to form bile pigment.
Biliverdin $C_{43}H_{54}N_4O_6$		Breakdown product of haemoglobin, reduced enzymatically in liver to bilirubin. Not found in blood, but present in bile of some animal placentas of some mammals (uteroverdin) and in egg shells of many birds (ovocyan). Also found in meconium of foetus and newborn at birth. An iron complex may be the prosthetic group of inactive liver catalase.
Mesobilirubin $C_{44}H_{58}N_4O_6$		May be present in the small intestine as reduction product of bilirubin.
Mesobilane (mesobilirubinogen, urobilinogen IX-a) $C_{44}H_{58}N_4O_4$		Degradation product of bilirubin in liver. Present in normal bile, urine and faeces, increase in pathological conditions.

Constituents of Living Matter – Porphyrins

Table 17 (continued) Bilirubinoids and related compounds

Substance	Structure	Remarks
Mesobilene-(b) (urobilin IX-α) $C_{33}H_{41}N_4O_4$		Oxidation product of mesobilane. in normal urine and faeces
(-)-Tetrahydro- mesobilane (stercobilinogen) $C_{33}H_{44}N_4O_4$		Reduction product of mesobilane excretory product of haemoglobin vertebrates
(-)-Tetrahydro- mesobilene-(b) (stercobilin) $C_{33}H_{44}N_4O_4$		Excretory product of haemoglobin faeces and urine
Mesobiliviolin $C_{33}H_{40}N_4O_4$		Found in human faeces, probably derived from mesobilane. Forms prosthetic group of the phycocyanins (chromoproteins and blue algae) that act as efficient photo- sensitizers in algal photosynthesis
Mesobilerythrin (mesobilirhodin) $C_{33}H_{40}N_4O_4$	Not established with certainty	Prosthetic group of phycoerythrin in some blue algae. A sensitizer in photosynthesis
Mesobilifuscins Bilifuscins Propiontydopentones $C_{14}H_{18-20}N_2O_4-5$	Not definitely established, but known to be dipyrroles containing the skeleton: 	Secondary products of oxidation of pigments and haem compounds, excreted in urine and faeces in jaundice and disease; present in gallstones
(+)-Urobilin $C_{33}H_{40}N_4O_5$	Not established with certainty. Strongly dextrorotatory	Isolated from infected bile, where it probably arises from bilirubin
(+)-Urobilinogen $C_{33}H_{42}N_4O_5$	Not established with certainty. Strongly dextrorotatory	Isolated from infected bile, where it probably arises from bilirubin

pids

Lipids is the general term for a group of natural products that are soluble in relatively nonpolar solvents, such as mixtures of

- (b) higher straight-chain alcohols, e.g., cetyl (C_{16}), stearyl (C_{18}), ceryl (C_{26}) and myrcyl (C_{20}) alcohols
- (c) sterols (see page 377), i.e., alcohols containing the cyclopentanoperhydrophenanthrene nucleus, e.g., cholesterol (see page 374), anosterol, stigmasterol and ergosterol
- (d) hydrocarbons, e.g., squalene (see page 374) and the carotenes
- (e) the fat-soluble vitamins A, D, E and K (see under "Vitamins", pages 457-469).

Further reading

DEERY, H. J., *The Lipids*, vol. I, Interscience, New York, 1951; HINGSTON, T. P., *The Chemical Constitution of Natural Fats*, 2nd ed., Butterworths, London, 1964; LORAN, J., *Lipids*, 1964; MCDONALD, I., *Lipids*, 1960; OLFORD, D. H., *Lipids*, 1960

taglandins (see page 373)

Table 18 Classification and structural components of saponifiable lipids

Classification of lipids*		Structural components (other than fatty acids)**		
		Ester or amide of	Nitrogenous base	Other
Acyl-glycerols (fats)	(i) Monoglycerides	Glycerol	—	—
	(ii) Diglycerides			
	(iii) Triglycerides (neutral fats)			
Alkoxydiglycerides		Glycerol	—	Higher aliphatic alcohols
Glycoglycerides		Glycerol	—	Galactose
Glycero-phosphatides	(i) Phosphatidic acids	Glycerol	—	Phosphoric acid
	(ii) Phosphatidyl esters	Phosphatidylcholine	Choline Ethanolamine Serine	Phosphoric acid
		Phosphatidylethanolamines		Phosphoric acid
		Phosphatidylserines		Phosphoric acid
	(iii) Lysophosphatides	Glycerol	Choline Ethanolamine Serine	Phosphoric acid
	(iv) Inositol phosphatides	Glycerol	—	Phosphoric acid, hexamethyl
	(v) Aceral phosphatides			
	(vi) Alkyl lysophosphatide ethers	Glycerol	(As for lymphopha- phatides) (As for lymphopha- phatides)	Phosphoric acid, unsaturated higher aliphatic alcohols Phosphoric acid, saturated higher aliphatic alcohols
Sphingo-lipids	(i) Sphingomyelins	Sphingosine and dihydrosphingosine	Choline	Phosphoric acid
	(ii) Cerebrosides		—	Hexose or disaccharide
	(iii) Sulphatides		—	Galactose, sulphuric acid
	(iv) Aminoglycolipids		N-Acetylglucosamine	Glucose, galactose
	(v) Gangliosides		N-Acetylglucosamine	Glucose, galactose, neuraminic acid
Waxes	(i) True waxes	Long-chain aliphatic alcohols Complex cyclic alcohols	—	—
	(ii) Steryl esters, vitamin A and D ₂ esters			

* See also Table 17, page 363.

Table 19 (continued) Fatty acids

Name	Formula and mol.wt.	Structure	Physical properties	Remarks
Lacceroic acid (dotriacontanoic acid)	$C_{31}H_{62}O_2$ 480.87	$CH_3(CH_2)_{30}COOH$	m.p. 96.2°C	Occurs in stick-lac wax (from <i>Tachardia latta</i>) and other natural waxes
<i>Unsaturated (mono-olefinic) straight-chain monocarboxylic acids</i>				
Acrylic acid (propenoic acid)	$C_3H_4O_2$ 72.06	$CH_2=CHCOOH$	m.p. 13°C b.p. 141°C d^{20}_4 1.062 n^{20}_D 1.4224	
<i>trans</i> -(α)-Crotonic acid (<i>trans</i> -butenoic acid)	$C_4H_6O_2$ 86.09	$CH_3CH=CHCOOH$	m.p. 72°C b.p. 189°C d^{20}_4 0.973 n^{20}_D 1.4228	Constituent of croton oil (from <i>Croton tiglium</i> seeds)
Iso-(β)-crotonic acid (<i>cis</i> -butenoic acid)	$C_4H_6O_2$ 86.09	$HCCH_3=CHCOOH$	m.p. 15.5°C b.p. 169°C d^{15}_4 1.0312 n^{20}_D 1.4457	Readily isomerizes to the <i>trans</i> -acid
Δ^4 -Hexenoic acid	$C_6H_{10}O_2$ 114.15	$CH_3(CH_2)_2CH=CHCOOH$	m.p. 32°C b.p. 217°C d^{20}_4 0.9627 n^{20}_D 1.4601	Occurs in Japanese peppermint oil
Δ^4 -Decenoic acid (obtusilic acid)	$C_{10}H_{18}O_2$ 170.25	$CH_3(CH_2)_4CH=CH(CH_2)_2COOH$	b.p. 148–150°C/13 d^{20}_4 0.9197 n^{20}_D 1.4497	Occurs in seed fat of <i>Lindera obtusiloba</i>
Δ^6 -Decenoic acid	$C_{10}H_{18}O_2$ 170.25	$CH_2=CH(CH_2)_7COOH$	b.p. 143–148°C/15 d^{15}_4 0.9238 n^{20}_D 1.4488	Occurs in butter and milk fats and in sperm head oil
Δ^4 -Dodecenoic acid (linderic acid)	$C_{12}H_{22}O_2$ 198.31	$CH_3(CH_2)_6CH=CH(CH_2)_2COOH$	m.p. 1–1.3°C b.p. 170–172°C/13 d^{20}_4 0.9081 n^{20}_D 1.4529	Occurs in various seed oils, e.g., <i>Lindera obtusiloba</i>
Δ^6 -Dodecenoic acid (lauroleic acid)	$C_{12}H_{22}O_2$ 198.31	$CH_3(CH_2)_5CH=CH(CH_2)_3COOH$	d^{15}_4 0.9130 n^{20}_D 1.4535	Occurs in sperm blubber and head oil
Δ^8 -Dodecenoic acid	$C_{12}H_{22}O_2$ 198.31	$CH_3CH_2CH=CH(CH_2)_7COOH$	—	Occurs in fat of cow's milk
Δ^6 -Tetradecenoic acid (tsuzuic acid)	$C_{14}H_{26}O_2$ 226.36	$CH_3(CH_2)_8CH=CH(CH_2)_2COOH$	m.p. 18–18.5°C b.p. 185–188°C/13 d^{20}_4 0.9024 n^{20}_D 1.4557	Occurs in various tropical plant oils, esp. tsuzu oil
Δ^6 -Tetradecenoic acid (physeteric acid)	$C_{14}H_{26}O_2$ 226.36	$CH_3(CH_2)_7CH=CH(CH_2)_3COOH$	d^{20}_4 0.9046 n^{20}_D 1.4552	Occurs in whale blubber and sardine oil
Δ^8 -Tetradecenoic acid (myristoleic acid)	$C_{14}H_{26}O_2$ 226.36	$CH_3(CH_2)_3CH=CH(CH_2)_7COOH$	d^{20}_4 0.9018 n^{20}_D 1.4549	Occurs in milk fat and depot and liver fat of many animals
Δ^8 -Hexadecenoic acid (palmitoleic acid)	$C_{16}H_{30}O_2$ 254.42	$CH_3(CH_2)_5CH=CH(CH_2)_7COOH$	m.p. 1°C b.p. 218–220°C d^{15}_4 0.9003	Widely distributed. In marine oils (15–20% of total fatty acids), in depot and milk fat of animals, vegetable oils and fats

Fatty acids

	Formula and mol wt	Structure	Physical properties	Remarks (for references see page 372)
ic d)	$C_{15}H_{31}O_2$ 282.47	$CH_3(CH_2)_9CH=CH(CH_2)_4COOH$	m p 32-33°C b p 208-210°C/10 d^{20}_4 0.8324 n^{20}_D 1.4535	Occurs in seeds of aromatic plants (parsley, celery, etc.) and in some umbellate fats
	$C_{17}H_{33}O_2$ 282.47	$CH(CH_2)_2COOH$ $ $ $CH(CH_2)_4CH_3$	m p. 13°C b p. 286°C/100 d^{20}_4 0.805 n^{20}_D 1.45823	Most abundant of the unsaturated fatty acids. Present in nearly all natural fats (one-third of fatty acids of cow's milk, phosphatides). Occurs in traces in human urine.
	$C_{17}H_{33}O_2$ 282.47	$CH_3(CH_2)_5CH=CH(CH_2)_7COOH$	m p 44-45°C b p. 288°C/100 d^{20}_4 0.851 n^{20}_D 1.4405	Formed by isomerization of oleic acid
id	$C_{17}H_{31}O_2$ 282.47	$CH_3(CH_2)_5CH=CHCH=CH(CH_2)_5COOH$	m p 42.5°C d^{20}_4 0.8560 n^{20}_D 1.4439	Occurs in many animal fats and vegetable oils
	$C_{17}H_{31}O_2$ 282.47	$CH(CH_2)_5COOH$ $ $ $CH(CH_2)_4CH_3$	m p 12.4-13°C	Has been shown to be the haemolytic acid occurring in plasma and various animal tissues. ¹ Also present in <i>Lactobacillus</i> species. ²
c	$C_{19}H_{37}O_2$ 282.47	$CH_3(CH_2)_4CH=CH(CH_2)_9COOH$	-	Occurs in partially hydrogenated peanut oil
	$C_{20}H_{39}O_2$ 310.52	$CH_3(CH_2)_7CH=CH(CH_2)_9COOH$	m p. 24.5°C	<i>Cis</i> and <i>trans</i> forms. In many fish and marine animal oils, in vegetable oils, in brain phosphatides
cid	$C_{19}H_{37}O_2$ 310.52	$CH_3(CH_2)_7CH=CH(CH_2)_9COOH$	m p <i>cis</i> 22°C <i>trans</i> 52-53°C	Principal acid of jojoba nuts ('goat nuts'), also in seed oil of <i>Ceanothus americanus</i> , rape- and mustard seed oils, fish oils
ic	$C_{20}H_{39}O_2$ 338.58	$CH_3(CH_2)_7CH=CH(CH_2)_9COOH$	m p 32-33°C	Occurs in various marine oils
id)	$C_{21}H_{41}O_2$ 338.58	$CH(CH_2)_8COOH$ $ $ $CH(CH_2)_7CH_3$	m p 33.5°C b p 281°C/30 d^{20}_4 0.860 n^{20}_D 1.4480	Occurs in seed oils, esp. rapeseed oil
id)	$C_{21}H_{39}O_2$ 338.59	$CH_3(CH_2)_8CH=CHCH=CH(CH_2)_7COOH$	m p 61.5°C b p 282°C/30 d^{20}_4 0.8565 n^{20}_D 1.4347	Formed by isomerization of erucic acid
	$C_{21}H_{39}O_2$ 366.63	$CH(CH_2)_8COOH$ $ $ $CH(CH_2)_7CH_3$	m p. 40.5-41°C n^{20}_D 1.4535	Occurs in shark and ray liver oils, in brain cerebrosides (nervone) and sphingomyelins. ³
	$C_{22}H_{41}O_2$ 354.67	$CH_3(CH_2)_8CH=CH(CH_2)_9COOH$	m p 45°C	Occurs in <i>Ximenia americana</i> (tallow-wood). A hexacosenoic acid is found with nervonic acid in brain cerebrosides.

Table 19 (continued) Fatty acids

Name	Formula and mol.wt.	Structure	Physical properties	Remarks
<i>Unsaturated (polyolefinic) straight-chain monocarboxylic acids</i>				
Sorbic acid ($\Delta^{2,4}$ -hexadienoic acid)	$C_8H_{10}O_2$ 112.13	$CH_3-CH=CH-CH=CH-COOH$	m.p. 134.5°C b.p. 228°C (decomp.)	Occurs as lactone in oil of unripe mulberries
Linoleic acid (<i>cis-cis</i> - $\Delta^{9,12}$ -octadecadienoic acid)	$C_{18}H_{32}O_2$ 280.45	$CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$	m.p. -11 (-5)°C b.p. 230°C/16 d^{20}_4 0.9025 n^{20}_D 1.4699	Widely distributed in plants, esp. in hemp and cottonseed oils. Also in lipids (component of phosphatides, etc.) a dietary component
Hiragonic acid ($\Delta^{8,10,14}$ -hexadecatrienoic acid)	$C_{16}H_{28}O_2$ 250.38	$CH_3-(CH_2)_2-CH=CH-CH_2-CH=CH-(CH_2)_4-COOH$	d^{20}_4 0.9288 n^{20}_D 1.4855	Occurs in sardine oil
α -Elcostearic acid (<i>cis</i> - $\Delta^{9,11,13}$ -octadecatrienoic acid)	$C_{18}H_{30}O_2$ 278.44	$CH_3-(CH_2)_2-(CH=CH)_3-(CH_2)_7-COOH$	m.p. 48°C b.p. 235°C/12 d^{20}_4 0.8980 n^{20}_D 1.5080	Occurs in vegetable oils, esp. tung oil
β -Elcostearic acid (<i>trans</i> - $\Delta^{9,11,13}$ -octadecatrienoic acid)	$C_{18}H_{30}O_2$ 278.44		m.p. 71°C d^{20}_4 0.8839 n^{20}_D 1.5000	Formed from α -elcostearic acid by action of light, heat and chemical reagents
Linolenic acid ($\Delta^{9,11,13}$ -octadecatrienoic acid)	$C_{18}H_{30}O_2$ 278.44	$CH_3-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$	m.p. -11.2 to -11°C b.p. 230-232°C/17 d^{20}_4 0.9046 n^{20}_D 1.4780	Occurs in many vegetable oils, esp. dry such as linseed oil. Also in traces in animal oils (phosphatides)
Stearidonic acid (morotric acid, $\Delta^{4,6,8,10}$ -octadecatetraenoic acid)	$C_{18}H_{30}O_2$ 276.42	$CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_4-COOH$	d^{20}_4 0.9297 n^{20}_D 1.4911	Occurs in fish oils. The position of the bonds is not confirmed
Timnodonic acid ($\Delta^{4,6,8,10,12,14}$ -eicosapentaenoic acid)	$C_{20}H_{30}O_2$ 302.46	$CH_3-CH=CH-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_4-COOH$	-	Occurs in sardine oil, cod-liver oil, pilot whale oil and oil from <i>Squalus suckleyi</i> (spiny dogfish)
Arachidonic acid ($\Delta^{6,8,10,12}$ -eicosatetraenoic acid)	$C_{20}H_{32}O_2$ 304.48	$CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_4-COOH$	m.p. -49.5°C n^{20}_D 1.8482	Occurs in fish oils. 'Essential' dietary linoleic acid
Clupanodonic acid ($\Delta^{4,6,8,10,12,14}$ -docosapentaenoic acid)	$C_{22}H_{34}O_2$ 330.52	$CH_3-CH_2-CH=CH-(CH_2)_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_4-COOH$	m.p. < -78°C b.p. 236°C/5 d^{20}_4 0.9290 n^{20}_D 1.4868	Occurs in fish oils
Nisinic acid ($\Delta^{4,6,8,10,12,14,16}$ -tetracosahexaenoic acid)	$C_{24}H_{36}O_2$ 356.55	$CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_4-COOH$	-	Occurs in tunny oil
Thynninic acid (Δ^7 -hexacosahexaenoic acid)	$C_{26}H_{40}O_2$ 384.61	-	d^{20}_4 0.9433 n^{20}_D 1.5022	Occurs in tunny oil

Is 19 (continued) Fatty acids

Name	Formula and mol wt	Structure	Physical properties	Remarks (for references see page 372)
<i>Unsaturated (acetylenic) straight-chain monocarboxylic acids</i>				
igric acid (6-stearolic acid, 6-octadecynoic acid)	$C_{18}H_{32}O_2$ 280.45	$CH_3(CH_2)_6C\equiv C(CH_2)_8COOH$	m p 50.5°C	Occurs in fat of <i>Pisammia</i> spp. (tariff) (bitter-bush oil)
erolic acid (9-octadecynoic acid)	$C_{18}H_{32}O_2$ 280.45	$CH_3(CH_2)_3C\equiv C(CH_2)_8COOH$	m p 48.5°C b p 260°C	Formed by oxidation of oleic or elaidic acid
ehenolic acid (13-docosynoic acid)	$C_{22}H_{40}O_2$ 336.56	$CH_3(CH_2)_9C\equiv C(CH_2)_8COOH$	m p 57.5°C	Formed by oxidation of erucic or brassidic acid
<i>Branched-chain monocarboxylic acids</i>				
sobutyric acid (2-methyl- propanoic acid)	$C_4H_8O_2$ 88.11	CH_3 \diagup CH_2 \diagdown $CHCOOH$	m p. -47°C b p 154.4°C d_{40}^{20} 0.949 n_D^{20} 1.393	Occurs free in carob beans (<i>Ceratonia siliqua</i>), as ethyl ester in croton oil, also in faeces and as product of enzymic breakdown of proteins. Intermediate in metabolism of valine (see page 396)
isovaleric acid (3-methylbutanoic acid)	$C_5H_{10}O_2$ 102.13	CH_3 \diagup CH_2 \diagdown CH_2COOH	m p -51°C b p 176.7°C d_{40}^{20} 0.937 n_D^{20} 1.50178	
Tiglic acid (<i>ac</i> -2-methyl-3-butenic acid)	$C_5H_{10}O_2$ 100.12	$CH_3CH=CHCOOH$	m p 64.5°C b p 198.5°C d_{40}^{20} 0.964 n_D^{20} 1.4342	Occurs in croton oil (glyceride); in Roman camellin oil (esters), in geranium oils. Intermediate in metabolism of isoleucine (see page 396)
Isomeric acid (13-methyltridecanoic acid)	$C_{14}H_{28}O_2$ 228.38	$CH_3CH(CH_3)_{12}COOH$	m p 51°C	Occurs together with other even-numbered <i>iso</i> acids from C_{12} to C_{44} as esters in wool wax ⁴
<i>anti</i> -Isomargaric acid (14-methyltridecanoic acid)	$C_{15}H_{30}O_2$ 270.46	$CH_3CH_2CH(CH_3)_{12}COOH$	m p 36.8°C [α] _D ²⁰ +5.2°	Occurs together with other odd-numbered <i>ante</i> - acids from C_{13} to C_{43} as esters in wool wax ⁴
Tuberculoelaidic acid (<i>n</i> -[...]-10-methyl-octadecanoic acid)	$C_{21}H_{40}O_2$ 298.51	$CH_3(CH_2)_9CH(CH_3)_{10}COOH$	m p 12.5-12.9 (23.5-25.8)°C b p 180°C/0.1 d_{40}^{20} 0.8771 n_D^{20} 1.4512 [α] _D ²⁰ -0.08°	Occurs free in lipids of tubercle bacilli and <i>Mycobacterium leprae</i> ⁴
Phytanic acid (3,7,11,15-tetramethylhexadecanoic acid)	$C_{26}H_{50}O_2$ 312.54	$CH_3CH_2CH(CH_3)_4CH_2CH(CH_3)_4CH_2CH(CH_3)_4CH_2CH(CH_3)_4COOH$	m p -6 to -7°C	Present in traces in animal fats, butter and in blood serum (increased in Refsum's syndrome) ⁴

Table 19 (concluded) Fatty acids

Name	Formula and mol.wt.	Structure	Physical properties	Remarks
Mycolipenic acid ([+]-2,4,6-trimethyltetracos-2-enoic acid)	$C_{27}H_{52}O_2$ 408.71	$CH_3(CH_2)_{17}\underset{\text{CH}_3}{\underset{ }{CH}}CH_2\underset{\text{CH}_3}{\underset{ }{CH}}CH=C\underset{\text{CH}_3}{\underset{ }{COOH}}$	-	One of the 3 phthioic acids of tuberc
Mycoceranic acid	$C_{27}H_{52}O_2$ 480.87	$CH_3(CH_2)_{22}\underset{\text{CH}_3}{\underset{ }{CH}}CH_2\underset{\text{CH}_3}{\underset{ }{CH}}CH_2\underset{\text{CH}_3}{\underset{ }{CH}}COOH$	-	In the lipids of tubercle bacilli ⁷

Hydroxy acids

α -Hydroxymyristic acid (2-hydroxytetradecanoic acid)	$C_{14}H_{28}O_3$ 244.38	$CH_3(CH_2)_{11}CH(OH)COOH$	m.p. 81-82°C	Occurs as esters in wool wax ⁴
α -Hydroxypalmitic acid (2-hydroxyhexadecanoic acid)	$C_{16}H_{32}O_3$ 272.43	$CH_3(CH_2)_{13}CH(OH)COOH$	m.p. 86°C [α] _D -1.0°	Occurs as esters in wool wax ⁴
α -Hydroxystearic acid (2-hydroxyoctadecanoic acid)	$C_{18}H_{36}O_3$ 300.49	$CH_3(CH_2)_{15}CH(OH)COOH$	m.p. 93°C	Minor component of cerebrosides of human brain
Ricinoleic acid (<i>cis</i> -12-hydroxy- Δ^9 -octadecenoic acid)	$C_{18}H_{34}O_3$ 298.47	$\underset{\text{CH}(CH_2)_1 COOH}{\underset{ }{CHCH_2}}CH(OH)(CH_2)_5CH_3$	m.p. 5, 7.7 and 16°C (3 forms) b.p. 250°C/15 n_D^{20} 1.4711 [α] _D ²⁰ +7.8°	As glyceride, chief constituent of castor oil
2-Hydroxytricosanoic acid	$C_{23}H_{46}O_3$ 370.62	$CH_3(CH_2)_{20}CH(OH)COOH$	-	Component of normal brain cerebrosides of about 7% of total fatty acids
Cerebronic acid (phrenosinic acid, 2-hydroxytetracosanoic acid)	$C_{24}H_{48}O_3$ 384.65	$CH_3(CH_2)_{21}CH(OH)COOH$	m.p. 90-93 (102)°C [α] _D ²² +3.33°	Component of cerebroside phrenobron. About 15% of total fatty acid cerebrosides ⁶
2-Hydroxynervonic acid (2-hydroxy- Δ^{18} -tetracosenoic acid)	$C_{24}H_{46}O_3$ 382.63	$CH_3(CH_2)_7CH=CH(CH_2)_{12}CH(OH)COOH$	m.p. 65°C [α] _D ²⁰ +2.87°	Component of cerebroside hydroxynervonic which the isomeric Δ^{17} -acid is also a component. About 12% of total fatty acids of brain

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(For references see page 377)

57

ids are aliphatic monocarboxylic acids, R COOH, where R is saturated or unsaturated, straight-chain or branched radical.



Unsaturated fatty acids with more than one double bond (poly-
enic or polyethenoic acids) play an important role in animal nutri-
tion, some are apparently not synthesized in the organism at a rate
sufficient to meet the requirements of growth and are therefore es-
sential constituents of the diet. The most important of these are *lin-*
oleic and *arachidonic* acids, the so-called 'essential fatty acids', the
ingestion of any of which is effective in preventing or curing the fat-
deficiency syndrome due to a completely fat free diet (see page 492)

P

trace amounts, e.g., elaidic acid (trans isomer of oleic
| vaccenic acid (trans-11-octadecenoic acid). Cis-trans geo-
isomerism is illustrated by the case of oleic and elaidic

Prostaglandins

trivial name	Formula and mol. wt.	Chemical name	Structure
glandin E ₁	C ₂₀ H ₃₂ O ₅ 354.49	11α,15-Dihydroxy-9-ketoprost- 13-enoic acid	
glandin E ₂	C ₂₀ H ₃₂ O ₅ 352.48	11α,15-Dihydroxy-9-ketoprost- 5,13-dienoic acid	
glandin F ₁	C ₂₀ H ₃₂ O ₅ 350.46	11α,15-Dihydroxy-9-ketoprost- 5,13,17-trienoic acid	
glandin F _{1α}	C ₂₀ H ₃₂ O ₅ 355.50	9α,11α,15-Trihydroxyprost- 13-enoic acid	
glandin F _{2α}	C ₂₀ H ₃₂ O ₅ 353.49	9α,11α,15-Trihydroxyprost- 5,13-dienoic acid	
glandin F _{2α}	C ₂₀ H ₃₂ O ₅ 351.47	9α,11α,15-Trihydroxyprost- 5,13,17-trienoic acid	

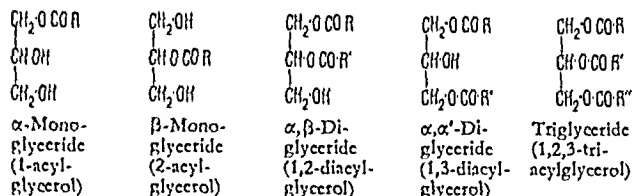
(For references see page 377)

Acylglycerols (fats)

The acylglycerols are formed by esterification of glycerol with one, two or three fatty-acid residues, yielding respectively a mono-, di- or triglyceride.

The natural fats are composed almost exclusively of triglycerides (neutral fats) together with traces of mono- and diglycerides. Lipids of the two latter types are formed during digestion and absorption of triglycerides and are found among the circulating lipids of the plasma.

At room temperature natural fats may be solid or liquid, and most contain at least 5 and up to 12 or more different fatty-acid residues. Chemically, they are complex mixtures of mixed triglycerides.



The tendency in all natural fats is towards maximum heterogeneity in the composition of the constituent triglycerides.

The fatty acids of most natural fats consist of mixtures of saturated and unsaturated acids. In general, the higher the proportion of saturated to unsaturated acids, the higher the melting point of the fat.

From the standpoint of their fatty-acid composition, the depot fats of land mammals are characterized by a preponderance of oleic acid, palmitic acid and in some important cases (e.g., ox, sheep) stearic acid. In the milk fat of land mammals this preponderance is diminished to an extent corresponding to the additional presence of the lower saturated fatty acids C_{12} down to C_4 (butyric acid). The depot fat of man contains the following percentages (by weight) of fatty acids: oleic 45, palmitic 25, linoleic 8, palmitoleic 7, stearic 6. The fats of aquatic animals contain mainly the higher unsaturated acids C_{18} to C_{22} together with usually 10-18% of palmitic acid.

Vegetable oils are often rich in the unsaturated C_{18} acids oleic ($C_{18:1}$), linoleic ($C_{18:2}$) and linolenic ($C_{18:3}$). The seed fats of the *Palmae* are rich in lower saturated fatty acids (e.g., 37-51% C_{12} , some C_{10} and C_8 in coconut oil), and the *Myristicaceae* yield much myristic acid (60-77% C_{14} in nutmeg oil).

In any particular tissue in the same species of animal the composition of the fat shows variations, and it is known that this is due at least in part to dietary differences. An example is the 'soft pork' produced from swine fed on soybean oil.

Absorption, transport and storage of fats

The dietary triglycerides, which contain long-chain or medium-chain fatty acids, are hydrolysed in the intestine by pancreatic lipase in the presence of conjugated bile salts to yield β -monoglycerides and free fatty acids. The β -monoglycerides may in small part be isomerized to their α -isomers. The reaction products, in the form of bile-salt micelles, are mainly absorbed in the upper gut. Both α - and β -monoglycerides are readily absorbed by the intestinal mucosa. A small part is hydrolysed and some is converted into phospholipids. The major portion, however, is directly acylated to triglycerides by enzymes present in the brush border or in the microsomes. This resynthesis of triglycerides is not a random process and certain fatty acids are preferred in given positions of the glycerol molecule. Medium-chain fatty acids are not re-esterified by the intestinal mucosa but transported via the portal circulation to the liver, where they are largely oxidized. Most of the reformed triglycerides pass from the villi via the lacteals, the intestinal lymphatics, the thoracic duct and the subclavian vein into the systemic blood stream, but a small portion may reach the liver via the portal circulation.

Blood fats. Fats are transported in the body by the blood stream in the form of fine droplets of 1 μ m or less in diameter known as *chylomicrons*. They are surrounded by a stabilizing film of protein (α - and β -globulins) and can be separated by centrifuging. The level of fats (and of other lipids) in the blood (see pages 590 sq.) rises after digestion of a meal containing fat. Hyperlipaemia also occurs after several days' fasting, when it is due to increased metabolism of depot fat following the exhaustion of glycogen reserves. Ingestion of alcohol, as well as the administration of various narcotics, also causes a marked increase in blood fats.

The chylomicrons are rapidly removed from the blood stream in the adipose tissue, heart muscle and liver. In the adipose tissue the triglycerides rapidly undergo considerable degradation, their constituent fatty acids are used for resynthesis of new glycerides and phospholipids and also for combustion to CO_2 . Since the body's capacity to metabolize the fatty acids is limited, drastic changes in the fatty-acid composition of dietary fats may affect that of the depot fats.

Depot fats. The principal locations of depot fats in the body are subcutaneous, intramuscular, in the omentum, and in association with various organs such as the heart, kidney, mesentery, ovaries etc. Their main function is that of an energy reserve, for which purpose they are more efficient than carbohydrates or proteins. In warm-blooded animals, subcutaneous fat often provides insulation against heat loss which is essential for survival. Adipose tissue also affords some protection against mechanical injury to important organs. In certain species, notably some marine animals, triglycerides are almost entirely replaced as energy reserves by other lipids for example waxes. In any particular animal the amount of depot fat laid down is dependent on the state of nutrition and other factors and it is being continuously utilized and replaced.

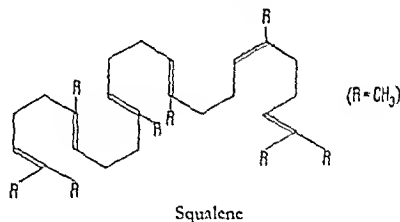
In addition to dietary fat, triglycerides synthesized in the body itself are also stored, the fatty acids arising from carbohydrates and thus indirectly also from proteins, and the glycerol mainly from the splitting of blood glucose.

Unsaponifiable matter of fats

Natural fats contain a proportion of *unsaponifiable matter* varying from 0.1 to 5%. This consists chiefly of cholesterol and other sterols, carotenoids (hydrocarbons related to carotene), and the fat-soluble vitamins (see pages 457-469). The reasons for the occurrence of these substances in natural fats are presumably their solubility in triglycerides and insolubility in water. Many fats contain steryl esters of fatty acids (see under 'Waxes', page 377) in addition to free sterols.

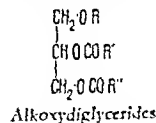
Cholesterol is a normal constituent of all animal tissues and a major constituent of brain and nerve tissue in particular. Dietary cholesteryl esters are hydrolysed in the intestine and the free sterol is absorbed by the brush border. It is then transferred to the mucosal cells by a displacement mechanism, re-esterified and transported to the lymph²⁵. Most of the body's cholesterol is synthesized endogenously, however, from acetyl-coenzyme A (see pages 426 to 427), principally in the liver. In the plasma, cholesterol circulates as a component of lipoproteins (see page 601).

The hydrocarbon *squalene* occurs in the liver oils of many elasmobranch fish, particularly sharks (up to 57% has been reported), also in olive oil, yeast fat and human skin. Its role as a precursor of cholesterol in the animal liver has been demonstrated (see page 426).



Alkoxydiglycerides

The liver oils of Elasmobranch fish contain considerable proportions of compounds differing from the triglycerides in containing an ether linkage. They are diglycerides in which the remaining hydroxyl group has formed an ether with a higher aliphatic alcohol ($\text{R}\cdot\text{OH}$) and may therefore be designated either as alkoxydiglycerides or as fatty acid esters of glyceryl ethers:



Ratfish liver oil consists almost exclusively of such compounds and contains practically no triglycerides. Diglyceride ethers of α, β -unsaturated higher aliphatic alcohols occur in the plasmalogen fraction (see page 376).

(For references see page 377)

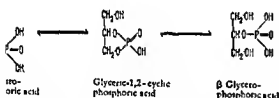
lycerides

olipids (phosphatides)

lly speaking, the phospholipids (phosphatides) are esters acids in which the alcohol component of the molecule

phosphatides

lycerophosphatides are of universal occurrence. Chemistry consist of α -glycerophosphoric acid esterified with fatty nd/or other constituents.

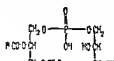


Phosphatide acids Phosphatide acids, the simplest of the ophosphatides and those most similar chemically to the trides are derived from α -glycerophosphoric acid

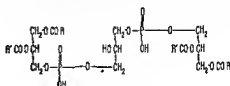


α Phosphatide acids
(where R, CO and R' CO are fatty acid residues)

osphatide acids have been isolated from a wide range of plant
e consisting of triglycerides in which one of the ester residues phosphatide acid¹⁰



A phosphatide acid derivative of importance is cardiolipin, which plays a role in the WASSERMANN reaction. First isolated from heart muscle, it consists of an α, α' -diglyceride in which the ester residues are both phosphatide acids¹¹.



Cardiolipin

The fatty acids of cardiolipin consist almost entirely of oleic and linoleic acids in the ratio 1:5. *E. coli* is capable of forming cardiolipin from α -phosphatidylglycerols¹².

(b) **Phosphatidyl esters** These substances are phosphatide acids esterified with the hydroxyl groups of ethanolamine, choline or serine:



Ethanolamine

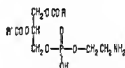


Choline

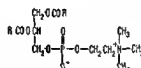


Serine

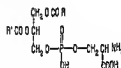
The resulting three types of phosphatidyl ester are



α -Phosphatidylethanolamines (cephalins)



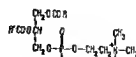
α -Phosphatidylcholines (lecithins)



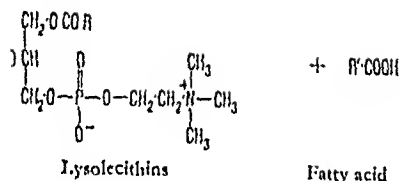
α Phosphatidylserines

The term 'cephalus' was originally given to an ethanol-insoluble
the term 'lecithin' was first used by Bloor in 1906 to designate the

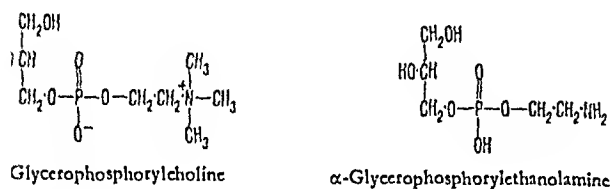
The lecithins obtained from many sources have all been shown
to have the same general structure



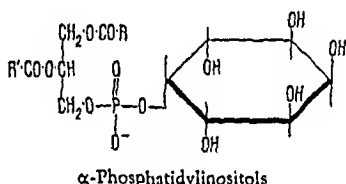
phospholipase A



(d) α -Glycerophosphoryl compounds that lack both of the fatty acids present in phosphatidyl esters occur in mammalian tissues and fluids¹⁶. They are α -glycerophosphorylethanolamine and α -glycerophosphorylcholine:



(e) *Phosphatidylinositides*¹⁶. At least three distinct inositides have been described. These have been differentiated on the basis of the ositol derivatives obtained on hydrolysis. One type, the phosphatidylinositols (phosphoinositides)¹⁷, are analogous to the glycerophosphatides. They occur in liver, heart, wheat germ and soybean, and have the following structure:

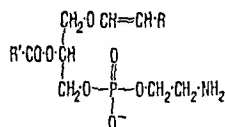


Di- and triphosphoinositides have a similar structure with, in addition, either one or two phosphoric acid groups esterified with an inositol moiety¹⁸.

Phosphoinositides are important metabolically active components of the myelin sheath, with a high turnover rate. They are found in neurokeratin and to peptides (phosphatidopeptides) containing β -alanine¹⁹.

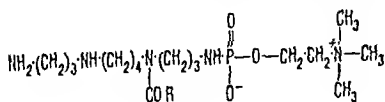
(f) *Acetal phosphatides* (plasmalogens). These compounds are closely related to the phosphatidyl esters. Plasmalogens containing ethanolamine (phosphatidyl ethanolamine) predominate in nature; compounds in which ethanolamine is replaced by either serine (phosphatidyl serine) or choline (phosphatidyl choline) are also widely distributed in many tissues. Phosphatidyl ethanolamine is the major ethanolamine-containing lipid of myelin.

Plasmalogens give a positive reaction for aldehydes, and the aldehydes corresponding to stearic and palmitic acids have been isolated from the crystalline acetal phosphatides of brain. About different aldehydic chains occur in plasmalogens, 25–35% of them branched²⁰. They have been shown²¹ to contain two β -chain alkyl groups, one of which is present in ester linkage and the other in an unsaturated vinyl ether linkage:



Acetal phosphatides (plasmalogens)

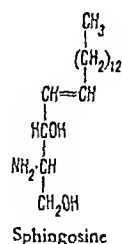
The existence of a phospholipid in malignant tumours has been reported. The compound, which possesses a marked affinity for topography III, is composed of choline, spermine, phosphoric acid and fatty acid. The following structure has been proposed²²:



(g) *Alkylxylylphosphatides*²¹. Analogues of acetal phosphatide with a saturated α,β -bond in the ethereal alkyl group, occur in myelin and other tissues. They may be regarded as alkyl ethers of lysophosphatides, e.g., glycerol 1-hexadecyloxy-2-acyl-3-phosphorylethanolamine. They lack aldehydic properties, resist some hydrolytic procedures, and are important components of the cephalin B complex of glycerophosphatides, which is difficult to separate from sphingomyelin.

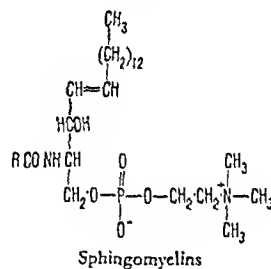
Sphingolipids

In the sphingolipid group, the base sphingosine (erythro-trans-1,3-dihydroxy-2-aminooctadec-4-ene) replaces glycerol. A single fatty acid radical is attached to the nitrogen by an amide linkage; the acylsphingosines are known as *ceramides*. Some sphingolipids are phosphatides, but others contain no phosphorus.



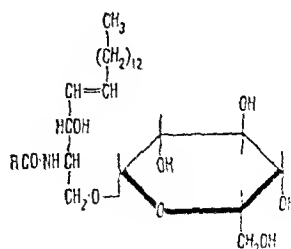
In some members of the sphingolipid group, sphingosine is replaced by dihydrosphingosine (in which the double bond of sphingosine is saturated), or by the 4-hydroxy derivative of dihydrosphingosine (1,3,4-trihydroxy-2-amino-octadecane), phytosphingosine or its C_{26} homologue.

(a) *Sphingomyelin*. The only sphingolipids resembling the glycerophosphatides are the sphingomyelins:



Sphingomyelin is an important component of the myelin sheath. The sphingomyelin of grey matter contains mainly stearic acid²², that of white matter mainly $\text{C}_{14:1}$ acid with lesser amounts of $\text{C}_{15:1}$, $\text{C}_{16:1}$, $\text{C}_{17:1}$, $\text{C}_{18:1}$ and $\text{C}_{19:1}$ acids.

(b) *Cerebrosides*²⁶. Cerebrosides are widely distributed in nature. They consist of ceramide attached by a β -glycosidic linkage to a sugar, usually galactose or glucose but sometimes a di- or trisaccharide. Myelin contains large amounts of galactocerebrosides (ceramide galactoside), separable into four classes on the basis of the fatty acid linked to sphingosine. A proportion of each galactocerebroside contains dihydrosphingosine in place of sphingosine.



Cerebrosides

Other fatty acids, ranging from C_{14} to C_{26} , as well as the corresponding α -hydroxy acids, also occur^{22,25}. The α -hydroxy acids constitute 50–60% of the total fatty acids.

Constituents of Living Matter - Lipids

Cerebroside	Constituent fatty acid
Kerasin	Lignoceric acid $\text{CH}_3(\text{CH}_2)_{22}\text{COOH}$
Phrenosin	Cerebronic acid $\text{CH}_3(\text{CH}_2)_{21}\text{CH}(\text{OH})\text{COOH}$
Nervone ,	Nervonic acid $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_{12}\text{COOH}$
Hydroxynervone	Hydroxynervonic acid $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_{11}\text{CH}(\text{OH})\text{COOH}$

In "True Waxes" distinction from "Fatty Acids" is made on the basis of their solubility in organic solvents. True waxes are insoluble in water and soluble in organic solvents, while fatty acids are soluble in water and insoluble in organic solvents.

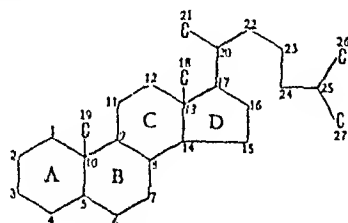
Waxes

The saponifiable waxes (as distinct from the hydrocarbons) are conveniently divisible into the so-called *true waxes*, which are long-chain fatty-acid esters of long-chain aliphatic alcohol.

Steroids

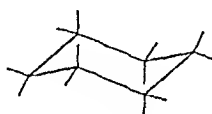
Stereochemistry

The naturally occurring steroids include the sex hormones, the adrenocortical hormones and progesterone as well as cholesterol and the bile acids. All steroids possess the cyclopentanoperhydrophenanthrene ring system, a fairly flat structure conveniently represented as planar:



Cyclopentanoperhydrophenanthrene ring system

The skeleton (nucleus) of the steroid molecule consists of three six-membered rings A, B and C and a five-membered ring D. Each of the six-membered rings is in the 'chair' conformation:

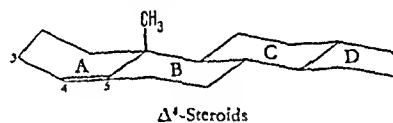


'Chair' conformation

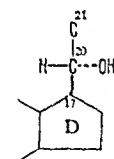
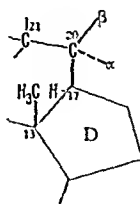
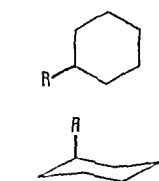
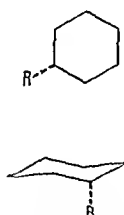
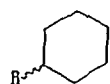
There may be methyl or other groups at C-10 and C-13 and a side chain at C-17 of up to eight carbons. In the oestrogens ring A is aromatic. The system of numbering is shown in the figure above.

In these structures all the carbon atoms shared by two rings are asymmetric and, in addition, replacement of hydrogen atoms on other carbon atoms by other monovalent groups introduces further asymmetry. Since the biological activity of steroids is dependent on the stereochemical configuration it is essential to give precise designations. In the skeleton as shown in the figure the side nearer the observer is designated ' β ' and the other side ' α '; thus in cholesterol the hydroxyl group projects towards the observer from the plane of the steroid skeleton when arranged as in the figure and so is 'above' it and thus ' β '. The systematic name for cholesterol is therefore cholest-5-en-3 β -ol. In structural formulae, groups with β configuration are shown as attached to the steroid skeleton by a continuous line (—), those with α configuration by a dotted or broken line (---). Groups of unknown configuration are shown attached by a wavy line (~~~~) and designated in names by the Greek letter. The prefix 'epi-' is used trivially to indicate inversion

or between C-5 and C-6, there is no hydrogen at C-5 and 1 stereoisomerism at the A:B ring junction. The prefix 'allo-' formerly used to denote the 5 α configuration. The C₁₇ steroid with 5 α configuration was formerly called coprostanone. 5 β configuration was called cholestane; the names 5 α -cholestan-3 β -ol and 5 β -cholestan-3 β -ol are now used. The C₁₉-steroid skeleton configuration was formerly called androstane while the 5 β variation was called aetiocholan-3 β -ol or actian-3 β -ol; they are now as 5 α -androstane and 5 β -androstane.

5 α series of steroids saturated at C-5

The symbols α and β are also used to denote stereoisomerism at C-20. For this purpose the carbon atoms C-20 and C-13 are assumed to lie in a plane parallel to and above the skeleton; valent groups attached to C-20 may then be either above this (β) or below it (α).

20 α -Hydroxy-20 β -Hyc β configuration
(R above the plane
of the ring) α configuration
(R below the plane
of the ring) ξ configuration
(configuration
unknown)

of a substituent; thus the more common natural form of oestradiol is the 17 β -hydroxy compound (17 β -oestradiol) while the less common 17 α -hydroxy form is often referred to as 17-epioestradiol or simply epioestradiol.

There are two distinct series of naturally occurring steroids saturated at C-5 which differ in their stereochemistry at the junction of the A and B rings. The series in which the A:B junction is *trans* is designated '5 α ' because the hydrogen attached to C-5 is on the α side and is *trans* with respect to the methyl group attached to C-10. The series in which the A:B junction is *cis* is designated '5 β ' because the hydrogen attached to C-5 is on the β side and is *cis* with respect to the methyl group attached to C-10. In steroids unsaturated at C-5, i.e., with a double bond between C-4 and C-5

Classification

Steroids are classified both by the total number of carbon in the molecule and according to their function (see opposite).

C₁₇-Steroids — parent compound *gonane*; no groups at C-10, or C-17.

C₁₈-Steroids — parent compound *estrane*; methyl group at C-10 and no side chain at C-17; include the naturally occurring oestrogens.

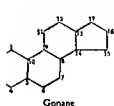
C₁₉-Steroids — parent compound *androstane*; methyl groups at C-10 and C-13 but no side chain at C-17; include the naturally occurring androgens.

Steroids – parent compound *pregnane*; methyl groups at C-10 and C-13 and a 2-carbon side chain at C-17, include the naturally occurring corticosteroids

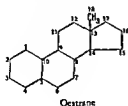
Stroids – parent compound *cholane*, methyl groups at C-10 and -13 and a branched 5-carbon side chain at C-17, include many naturally occurring bile acids

Steroids – parent compound *cholestane*, methyl groups at C-10 and C-13 and a branched 8-carbon side chain at C-17, e.g., cholesterol.

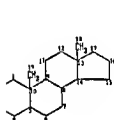
Names of parent compounds of other naturally occurring steroids: *ergostane* (24-methyl-5 α -cholestane), *stigmastane* (24-ethyl-5 α -cholestane), *lanostane* (4,4,14 α -trimethyl-5 α -cholestane)



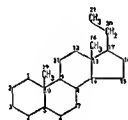
Gonane



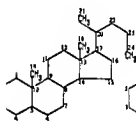
Estrane



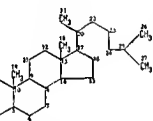
Androstane



Pregnane



Cholane



Cholestane

ble 21 Prefixes and suffixes in steroid nomenclature

Chemical group	Prefix	Suffix
double bond	Δ (in trivial names only)	changes -ane to -ene
triple bond	–	changes -ane to -yne
hydroxyl	hydroxy-	-ol
acetate ester	acetoxy-	-yl acetate
benzoate ester	benzyloxy-	-yl benzoate
sulphate ester	–	-yl sulphate
glucuronoside (glucuronide)	–	-glucuronide
carbonyl	oxo- (formerly keto-)	-one
aldehyde	–	-al
carboxylic acid	carboxy-	-oic acid
amine	amino	-amine
halogen (e.g., chlorine)	halogeno- (e.g., chloro-)	halide (e.g., chloride, in trivial names only)
epoxide	epoxy-	–
ethyne (–C \equiv CH)	ethynyl-	–

Systematic nomenclature

Steroids are named systematically² by adding prefixes and suffixes to the names of the parent hydrocarbons. The Greek letter Δ was formerly used to denote an olefinic double bond and is still

monal activity.

Prefixes and suffixes used in steroid nomenclature are listed in Table 21.

Other prefixes in trivial or systematic use are

allo- (in trivial names): formerly used to denote the 5 α -series of saturated steroids

anhydro- (in trivial names): loss of H and OH from adjacent carbon atoms with formation of a double bond

dehydro- (in trivial names): loss of 2H from adjacent carbon atoms with formation of a double bond

deoxy- or *desoxy-* (in trivial names): replacement of OH by H

de-: removal of a whole ring, e.g., de-D

dihydro- (in trivial names): addition of 2H to a double bond

epi- (in trivial names): inversion of a substituent from α to β or from β to α

homo-: ring enlargement, e.g., D-homo- means a six membered D ring

nor- (preceded by carbon number or ring letter): removal of one carbon atom

neo-: ring fission with addition of one H to each of the two terminal groups (preceded by the numbers of the atoms forming the bond cleaved)

Steroid hormones

Steroid hormones are found in all classes of vertebrates³ and

Table 22 Names, formulae and hormonal activity of important steroids

Trivial name	Systematic name	Formula (mol. wt.)	Hormonal activity*
<i>Adrenosterone</i>	Androst-4-ene-3,11,17-trione	$C_{19}H_{30}O_3$ (300.40)	♂
<i>Aetianedione</i> (aetiocholanedione) ..	5β-Androstane-3,17-dione	$C_{19}H_{30}O_2$ (288.43)	-
<i>Aetiocholanolone</i>	3α-Hydroxy-5β-androstan-17-one	$C_{19}H_{30}O_2$ (290.45)	-
3β- <i>Aetiocholanolone</i>	3β-Hydroxy-5β-androstan-17-one	$C_{19}H_{30}O_2$ (290.45)	-
<i>Aldosterone</i>	11β,21-Dihydroxypregn-4-en-18-al-3,20-dione	$C_{21}H_{34}O_6$ (360.45)	G, M
<i>Allocortol</i>	5α-Pregnane-3α,11β,17α,20α,21-pentol	$C_{21}H_{38}O_5$ (368.52)	-
β- <i>Allocortol</i>	5α-Pregnane-3α,11β,17α,20β,21-pentol	$C_{21}H_{38}O_5$ (368.52)	-
<i>Allocortolone</i>	3α,17α,20α,21-Tetrahydroxy-5α-pregnan-11-one	$C_{21}H_{38}O_5$ (366.50)	-
β- <i>Allocortolone</i>	3α,17α,20β,21-Tetrahydroxy-5α-pregnan-11-one	$C_{21}H_{38}O_5$ (366.50)	-
α- <i>Allopregnanediol</i>	3α,20α-Dihydroxy-5α-pregnane	$C_{21}H_{38}O_2$ (320.52)	-
β- <i>Allopregnanediol</i>	3β,20α-Dihydroxy-5α-pregnane	$C_{21}H_{38}O_2$ (320.52)	-
α- <i>Allopregnanolone</i>	3α-Hydroxy-5α-pregnan-20-one	$C_{21}H_{36}O_2$ (318.50)	-
<i>Allotetrahydrocortisol</i>	3α,11β,17α,21-Tetrahydroxy-5α-pregnan-20-one	$C_{21}H_{38}O_5$ (366.50)	-
<i>Androstenedione</i>	5α-Androstane-3,17-dione	$C_{19}H_{28}O_2$ (288.43)	♂
<i>Androstenedione</i>	Androst-4-ene-3,17-dione	$C_{19}H_{28}O_2$ (286.42)	♂
<i>Androsterone</i>	3α-Hydroxy-5α-androstan-17-one	$C_{19}H_{30}O_2$ (290.45)	♂
<i>Betamethasone</i> **	9α-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione	-	G, A
<i>Cholecalciferol</i>	See Vitamin D ₃		
<i>Cholesterol</i>	Cholest-5-en-3β-ol	$C_{27}H_{48}O$ (386.67)	-
<i>Cortexolone</i>	See 11-Deoxycortisol		
<i>Cortexone</i>	See Deoxycorticosterone		
<i>Corticosterone</i>	11β,21-Dihydroxypregn-4-ene-3,20-dione	$C_{21}H_{30}O_4$ (346.47)	G, M
(compound B)			
<i>Cortisol</i>	11β,17α,21-Trihydroxypregn-4-ene-3,20-dione	$C_{21}H_{30}O_5$ (362.47)	G, A, M
(hydrocortisone, 17α-hydroxy-corticosterone, compound F)			
<i>Cortisone</i>	17α,21-Dihydroxypregn-4-ene-13,11,20-trione	$C_{21}H_{30}O_5$ (360.45)	G, A, M
(compound E)			
α- <i>Cortol</i>	5β-Pregnane-3α,11β,17α,20α,21-pentol	$C_{21}H_{38}O_5$ (368.52)	-
β- <i>Cortol</i>	5β-Pregnane-3α,11β,17α,20β,21-pentol	$C_{21}H_{38}O_5$ (368.52)	-
α- <i>Cortolone</i>	3α,17α,20α,21-Tetrahydroxy-5β-pregnan-11-one	$C_{21}H_{38}O_5$ (366.50)	-
β- <i>Cortolone</i>	3α,17α,20β,21-Tetrahydroxy-5β-pregnan-11-one	$C_{21}H_{38}O_5$ (366.50)	-
11- <i>Dehydrocorticosterone</i>	21-Hydroxypregn-4-ene-3,11,20-trione	$C_{21}H_{28}O_4$ (344.45)	G
(compound A)			
<i>Dehydroepiandrosterone</i>	3β-Hydroxyandrost-5-en-17-one	$C_{19}H_{28}O_2$ (289.44)	♂
(dehydroisoandrosterone, androsthenolone)			
<i>Deoxycorticosterone</i>	21-Hydroxypregn-4-ene-3,20-dione	$C_{21}H_{30}O_3$ (330.47)	G
(11-deoxycorticosterone, DOC, cortexone, 21-hydroxypregnenolone)			
11- <i>Deoxycortisol</i>	17α,21-Dihydroxypregn-4-ene-3,20-dione	$C_{21}H_{30}O_4$ (346.47)	G
(cortexolone, substance S)			
21- <i>Deoxycortisol</i>	11β,17α-Dihydroxypregn-4-ene-3,20-dione	$C_{21}H_{30}O_4$ (346.47)	-
<i>Dexamethasone</i> **	9α-Fluoro-16α-methyl-11β,17α,21-trihydroxypregna-1,4-diene-3,20-dione	$C_{22}H_{28}FO_5$ (392.47)	A, G
<i>Epiandrosterone</i>	3β-Hydroxy-5α-androstan-17-one	$C_{19}H_{30}O_2$ (290.45)	♂
(isoandrosterone)			

* A Anti-inflammatory activity
G Glucocorticoid activity

M Mineralocorticoid activity
P Progestational activity

♂ Androgenic activity
♀ Oestrogenic activity

** Synthetic steroid; no known natural occurrence.

Table 22 Names, formulae and hormonal activity of important steroids

Trivial name	Systematic name	Formula (mol wt)	Hormonal activity*
<i>Epiestradiol</i> ... (17-epioestradiol, oestradiol-17 α)	Oestra-1,3,5(10)-triene-3,17 α -diol	C ₁₈ H ₁₈ O ₂ (272.39)	♀
<i>Epitestosterone</i> ...	17 α -Hydroxyandrost-4-en-3-one	C ₁₉ H ₁₈ O ₂ (288.43)	-
<i>Equilenin</i> ...	3-Hydroxyoestra-1,3,5(10),6,8-penten-17-one	C ₁₈ H ₁₈ O ₂ (266.34)	♀
<i>Equilin</i> ...	3-Hydroxyoestra-1,3,5(10),7-tetraen-17-one	C ₁₈ H ₁₈ O ₂ (268.36)	♀
<i>Ergocalciferol</i> ...	See Vitamin D ₂		
<i>Ergosterol</i> ...	24-Methylcholesta-5,7,22-trien-3 β -ol	C ₂₈ H ₄₈ O (396.66)	-
<i>Ethinylestradiol</i> **	17 α -Ethinylestra-1,3,5(10)-triene-3,17 β -diol	-	♀
<i>Fluorocortisol</i> ** (9 α -fluorocortisol, 9 α -fluoro- hydrocortisone)	9 α -Fluoro-11 β ,17 α ,21-trihydroxypregna-4-ene-3,20-dione	-	A, M†
<i>Fluorometholone</i> ** (oxylone)	9 α -Fluoro-6 α -methyl-11 β ,17 α -dihydroxypregna-1,4-diene-3,20-dione	-	A
<i>Fluoxymetstone</i> **	9 α -Fluoro-11 β ,17 β -dihydroxy-17 α -methylandrost-4-en-3-one	-	♂
17 α -Hydroxypregsterone	17 α -Hydroxypregna-4-ene-3,20-dione	C ₂₁ H ₃₀ O ₂ (330.47)	♂, P
20 α -Hydroxypregsterone	20 α -Hydroxypregna-4-en-3-one	C ₂₁ H ₃₀ O ₂ (316.49)	P
20 β -Hydroxypregsterone	20 β -Hydroxypregna-4-en-3-one	C ₂₁ H ₃₀ O ₂ (316.49)	P
<i>Lanosterol</i>	4,4,14 α -Trimethylcholesta-8,24-dien-3 β -ol	C ₂₈ H ₄₈ O (426.73)	-
<i>Methylprednisolone</i> **	6 α -Methyl-11 β ,17 α ,21-trihydroxypregna-1,4-diene-3,20-dione	C ₂₁ H ₂₈ O ₂ (374.48)	A, M†
<i>Norethandrolone</i> **	17 α -Ethyl-17 β -hydroxy-19-norandrost-4-en-3-one	-	♂***
<i>Norethandrone</i> ** (norethisterone)	17 α -Ethinyl-17 β -hydroxy-19-norandrost-4-en-3-one	-	P
<i>Norethynodiol</i> **	17 α -Ethinyl-17 β -hydroxyoestra-5(10)-en-3-one	-	P
<i>Oestradiol</i> (oestradiol-17 β)	Oestra-1,3,5(10)-triene-3,17 β -diol	C ₁₈ H ₁₈ O ₂ (272.39)	♀
<i>Oestrinol</i>	Oestra-1,3,5(10)-triene-3,16 α ,17 β -triol	C ₁₈ H ₁₈ O ₂ (288.39)	♀
<i>Oestrone</i>	3-Hydroxyoestra-1,3,5(10)-trien-17-one	C ₁₈ H ₁₈ O ₂ (270.37)	♀
<i>Prednisolone</i> **	11 β ,17 α ,21-Trihydroxypregna-14-diene-3,20-dione	C ₂₁ H ₂₈ O ₂ (360.45)	A, M†
<i>Prednisone</i> **	17 α ,21-Dihydroxypregna-1,4-diene-3,11,20-trione	C ₂₁ H ₂₈ O ₂ (358.44)	A, M†
<i>Pregnandiol</i>	5 β -Pregnane-3 α ,20 α -diol	C ₂₇ H ₄₈ O ₂ (320.52)	-
<i>Pregnantisol</i>	5 β -Pregnane-3 α ,17 α ,20 α -triol	C ₂₇ H ₄₈ O ₂ (336.52)	-
<i>Pregnenolone</i>	3 α -Hydroxy-5 β -pregnan-20-one	C ₂₇ H ₄₈ O ₂ (318.50)	-
<i>Pregnenolone</i> (Δ^4 -pregnenolone)	3 β -Hydroxypregna-5-en-20-one	C ₂₇ H ₄₈ O ₂ (316.49)	-
<i>Pregsterone</i>	Pregna-4-ene-3,20-dione	C ₂₁ H ₃₀ O ₂ (314.47)	P
<i>Testosterone</i>	17 β -Hydroxyandrost-4-en-3-one	C ₁₉ H ₂₈ O ₂ (288.43)	♂
<i>Tetrahydro-A</i>	3 α ,21-Dihydroxy-5 β -pregnane-11,20-dione	C ₂₇ H ₄₈ O ₂ (348.49)	-
<i>Tetrahydro-B</i>	3 α ,11 β ,21-Trihydroxy-5 β -pregnan-20-one	C ₂₇ H ₄₈ O ₂ (350.50)	-
<i>Tetrahydro-E</i>	See Urocortisone		
<i>Tetrahydro-F</i>	See Urocortisol		
<i>Tetrahydro-G</i>	3 α ,17 α ,21-Trihydroxy-5 β -pregnan-20-one	C ₂₇ H ₄₈ O ₂ (350.50)	-
<i>Triamcinolone</i> **	9 α -Fluoro-11 β ,16 α ,17 α ,21-tetrahydroxypregna-1,4-diene-3,20-dione	C ₂₁ H ₂₆ FO ₂ (394.44)	A
<i>Ursadisterone</i>	3 α ,11 β ,21-Trihydroxy-20-oxo-5 β -pregnan-18-al	C ₂₇ H ₄₆ O ₂ (364.49)	-
<i>Urocortisol</i> (tetrahydro-F)	3 α ,11 β ,17 α ,21-Tetrahydroxy-5 β -pregnan-20-one	C ₂₇ H ₄₈ O ₂ (366.49)	-
<i>Urocortisone</i> (tetrahydro-E)	3 α ,17 α ,21-Trihydroxy-5 β -pregnane-11,20-dione	C ₂₇ H ₄₈ O ₂ (364.47)	-
1 α -Steroid D ₁ (ergocalciferol)	24-Methyl-9,10-secocholesta-5,7,10(19),22-tetraen-3 β -ol	C ₂₈ H ₄₄ O (396.66)	-
1 α -Steroid D ₂ (cholecalciferol)	9,10-Seccocholesta-5,7,10(19)-trien-3 β -ol	C ₂₈ H ₄₄ O (384.65)	-

* A Anti-inflammatory activity
G Glucocorticoid activity

M Mineralocorticoid activity
P Progesterone activity

♂ Androgenic activity
♀ Oestrogenic activity

** Synthetic steroid, no known natural occurrence
*** High anabolic activity, low androgenic activity

Enzymes

Enzymes are protein catalysts ranging in molecular weight from about 13 000 (ribonuclease) up to as much as one million (pyruvate decarboxylase). They are purified and isolated by the use of techniques for fractionating proteins¹. Their general properties will be described in the section which follows².

Nomenclature of enzymes

Enzymes are usually given names indicating both the principal substrate and the reaction catalysed (e.g., malate dehydrogenase). Many enzymes have, however, been given trivial names and these are often a cause of confusion. With the aim of eliminating the existing ambiguity, the Commission on Enzymes of the International Union of Biochemistry has worked out a systematic nomenclature² based on the reaction catalysed (see Table 24, page 385) and has given each enzyme a characteristic number indicating the nature of this reaction together with a recommended trivial name (these names have been used in the chapter on 'Metabolism' on pages 387-445).

The word 'enzyme' usually denotes a catalytic protein plus any component that cannot be readily removed from the protein without denaturing it. The usage is not very rigid, however, for in some contexts 'enzyme' is intended to include dissociable cofactors and in others to indicate the catalytic protein *per se*. If there is danger of ambiguity, the catalytic protein is denoted by the term '*apo-enzyme*' and the protein plus cofactors by '*holo-enzyme*'.

Coenzymes or *prosthetic groups* are nonprotein organic compounds which, in combination with the apo-enzyme, play an intimate part in the catalysis by the enzyme. There is no generally accepted distinction between coenzymes and prosthetic groups, but the latter name is usually reserved for groups that are bound relatively firmly by the protein. '*Activators*' are usually distinguished from coenzymes in being small ions that are required by some enzymes for full catalytic activity. Some enzymes do not appear to possess a prosthetic group or coenzyme nor do they require an activator.

Specificity of enzymes³

Although nearly all the individual reactions of intermediary metabolism are catalysed by separate enzymes (see pages 405-419), few of these enzymes are absolutely specific to the structure of their substrates. Most enzymes can act on close structural analogues of their physiological substrates, although usually at much reduced rates, whilst a few enzymes can act on a relatively wide group of substrates. Like any other catalyst, an enzyme catalyses both the forward and reverse reactions, but does not affect the final position of the equilibrium.

There are no completely general rules of enzyme specificity, for in different enzyme systems different parts of the substrate molecule appear to be important. Thus, the lipases require an ester bond in their substrates but there can be very considerable variation in the structures of the groups adjoining this susceptible bond. On the other hand, chymotrypsin and trypsin require certain configurations in the neighbourhood of the susceptible bond, but the nature of the bond itself can vary. For example, these enzymes will hydrolyse peptide bonds in protein substrates but in certain artificial substrates (e.g., methyl cinnamate) ester bonds can be hydrolysed.

An added complication is that those hydrolytic enzymes which can act on several substrates are usually capable of catalysing a transferring reaction in which an alcohol or an amine replaces the water. Many of these transfer reactions are unlikely to be of physiological significance because of the prevalence of water molecules under physiological conditions.

Many enzymes show stereochemical specificity in being unable to attack geometrical or optical isomers of their substrates. Less specific enzymes such as the esterases can, however, attack stereochemical isomers although usually at reduced rates.

Structure of enzymes and mechanism of enzyme action

In 1963 the complete sequence of the 124 amino-acid residues, together with the position of the sulphur bridges in the chain, was established for bovine ribonuclease⁴. Since that time the amino-acid sequence of many other enzymes has been elucidated²². The three-dimensional structure (conformation) of a few enzymes (e.g.,

lysozymes, ribonuclease, α -chymotrypsin) in the crystalline state has been determined by X-ray diffraction²³. In 1969 the first synthesis of an enzyme, that of ribonuclease, was accomplished.

It is now clear that the full catalytic activity of an enzyme depends on the integrity of the three-dimensional structure of the folded polypeptide chain. Denaturation of the enzyme, with concomitant destruction of the organization in the chain will usually result in loss of enzyme activity. The surface formed by the folding of the chain in the native structure thus enables the substrate molecules to combine with the enzyme at three or more points. Those amino-acid residues which contribute towards the formation of the enzyme-substrate complex and which take part in the catalytic process together constitute the 'active site' of the enzyme⁵. The folding of the peptide chain thus brings amino-acid residues which are remote from each other in sequence into close juxtaposition at the active site. Although the complete structures are unknown, the amino-acid sequences near the active sites of many enzymes have been determined (e.g., cytochrome c, trypsin, pancreatic phosphoglucomutase). Studies of this type reveal variations in the amino-acid sequences in the same enzyme from different species (e.g., ribonuclease)⁶. Some enzymes, for example those involved in biosynthetic pathways, appear to have two distinct active sites, one for combining with substrate and another for combining with an inhibitor⁷ which may regulate the biological action of the enzyme. It is suggested that the formation of a complex between the inhibitor and the enzyme induces a conformational change in the enzyme structure that modifies the catalytic activity of the other active site rendering the enzyme inactive. This class of proteins have been called 'allosteric'⁸.

Although there is no instance in which the mechanism of action of an enzyme is fully understood, a large number of mechanisms have been proposed⁹. The most attractive ideas involve the formation of a covalently-bound enzyme-substrate compound in which nucleophilic or electrophilic attack on the substrate molecule is facilitated by the enzyme.

Enzyme kinetics¹⁰

When an enzyme is added to a suitable reaction mixture there is first a very short lag before a steady rate of reaction is attained¹¹. This lag is so short that it is not detectable when the rate is obtained from measurements made at intervals of one minute or longer. Once established, the rate remains constant for a period which may sometimes be as long as several hours, although in other cases it may be only a few minutes. The rate of reaction begins to fall after this period because of reduced substrate concentration and/or the accumulation of products. This decrease in reaction rate is not easily analysed mathematically, and it is therefore usual to study only the constant reaction rate. The following discussion is confined to this constant reaction rate.

If the enzyme is susceptible to inhibition by excess substrate (see below) the rate may at first increase as the inhibition is relieved by removal of the substrate.

Enzyme concentration. The reaction rate is usually proportional to the concentration of enzyme. Strict linearity may not always be achieved experimentally, for instance because the enzyme preparation may contain a dissociable activator or inhibitor or the enzyme may be unstable at low concentrations. Alternatively, the reaction may have proceeded so far that the rate has already commenced to fall off at the highest enzyme concentrations.

Hydrogen-ion concentration. Most enzymes possess well-defined pH optima with appreciable activity over a range of only 2-3 pH units. Some enzymes are inhibited by one or other of the buffers in common use. It is therefore often worthwhile to compare the results in one buffer with those obtained in another type of buffer solution of the same pH range.

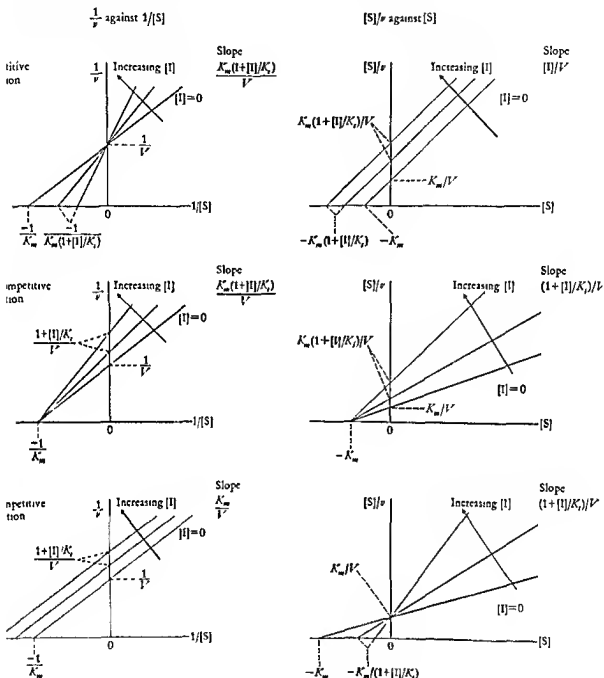
The study of kinetic data obtained at different pH values with different substrates and different concentrations of a single substrate is of use in investigating the details of enzyme mechanisms¹². For other purposes, the variations in the pH curve with different substrates and substrate concentrations are not usually important.

Temperature. The rate of an enzyme-catalysed reaction increases by a factor which is usually 1.5-3 for every rise of 10°C. There is, however, an optimum temperature above which further increase reduces the amount of substrate reacting because the enzyme becomes inactivated. The optimum temperature for short-term experiments (e.g., of one hour's duration) is often about 50°C. Most

* The enzymes occurring in blood and various body tissues are described on pages 584-600, those responsible for digestion on pages 405-419. On enzyme units see page 584.

Inhibition data plotted according to Table 23

Each line represents data for a series of substrate concentrations. One line of each graph is without inhibition and the other two are for two different concentrations of inhibitor



human enzymes show little inactivation in the presence of cofactors and substrates at 37°C , so that this is usually a safe temperature to study the reaction. It is not desirable to raise the temperature to the optimum because the rate of denaturation, and therefore the optimum temperature, is often influenced by slight changes in the experimental conditions.

Substrate concentration. As the initial substrate concentration is varied, the rate of reaction is at first proportional to this concentration, but at higher values it usually becomes virtually independent of it. This relation can be justified theoretically by considering a mechanism such as

concentration of enzyme present. K_m is given by $(k_{-1} + k_2)/k_1$ and has the dimensions of concentration. Although K_m is independent of both $[S]$ and t , it usually changes with pH, temperature, different substrates and the cofactor concentration. K_m may sometimes change with ionic strength or with different buffers and, like other characteristics of enzymes, it may differ for similar enzymes from different sources.

Equation (2) was first obtained theoretically by MICHAELIS and MENTEN¹², who assumed that the second reaction of mechanism (1) was the rate-limiting step. Under these conditions k_{-1} is much greater than k_2 , and K_m becomes k_{-1}/k_1 , which is the dissociation constant of the enzyme-substrate compound. This assumption is known to be valid for some enzymes but not for others¹⁴.

Evaluation of Michaelis constant K_m and maximum velocity V . K_m may be evaluated by plotting the curve of v against $[S]$. The experimental data can, however, be used more efficiently by plotting certain functions of v and $[S]$ as shown in Table 23^{3,15}. These plots give straight lines if equation (2) is obeyed. The plot of $1/v$ against $1/[S]$ has the advantage that the variables are separate and the calculations for plotting are thus quicker. Unfortunately the points are not evenly spread and the errors at low values of v are accentuated. This method gives accurate values for V but less accurate estimates for K_m . A statistical evaluation¹⁶ of the various graphical methods for determining K_m and V shows that the third method (Table 23) is the most satisfactory and gives the most accurate values of these quantities over the usual range of concentration and velocity available for experimentation.

Table 23 Linear plots for evaluating MICHAELIS constant K_m and maximum velocity V

Plot		Slope	Intercept	
Ordinate	Abcissa		Ordinate	Abcissa
$1/v$	$1/[S]$	K_m/V	$1/V$	$-1/K_m$
v	$v/[S]$	$-K_m$	V	V/K_m
$[S]/v$	$[S]$	$1/V$	K_m/V	$-K_m$

It is sometimes convenient, such as when comparing different substrates, to plot v against $\log [S]$. This plot gives an S-shaped curve instead of a straight line; the inflection of this curve occurs at a value of $\log [S]$ equal to $\log K_m$.

Inhibition by excess substrate. This phenomenon occurs with some enzymes and is usually explained by postulating that the enzyme-substrate compound (ES) combines with a second molecule of S to form an inactive complex which, unless it reverts to the original ES form, can yield products only slowly or not at all. When v is plotted against $\log [S]$, this mechanism predicts a symmetrical bell-shaped curve¹⁷ if the rate can be reduced to zero by high substrate concentrations. This prediction agrees with experimental findings¹⁸.

Another mechanism of substrate inhibition may occur if there is a dissociable cofactor such as Mg^{++} which can combine with the substrate. Increased substrate concentration may inhibit by removing the cofactor.

Inhibitors¹⁵. Two types of inhibition are commonly encountered, competitive and noncompetitive. In the competitive type, the inhibition is reduced by increasing the concentration of substrate. Many competitive inhibitors are structural analogues of the substrate, suggesting that the inhibitor and the substrate combine with the same site of the enzyme. Assuming that the inhibitor can react reversibly with the enzyme so as to prevent it combining with its substrate, it can be derived that on the basis of mechanism (1):

$$v = \frac{V[S]}{K_m(1 + [I]/K_i) + [S]} \quad (3)$$

where $[I]$ is the concentration of inhibitor and K_i is the dissociation constant of the enzyme-inhibitor compound. V and K_m are the values obtained in the absence of the inhibitor.

In a case of noncompetitive inhibition, the amount of inhibition is independent of the concentration of substrate and depends only on the concentration of inhibitor. An equation to fit this can be derived by assuming that the inhibitor combines reversibly and equally readily with both the enzyme and the enzyme-substrate compound:

$$v = \frac{V[S]}{(K_m + [S])(1 + [I]/K_i)} \quad (4)$$

This mechanism suggests that a noncompetitive inhibitor does not combine with the active centre of the enzyme responsible for combination with the substrate.

It should be noted that, in competitive inhibition, the inhibitor increases the apparent MICHAELIS constant without affecting the maximum velocity, whereas in noncompetitive inhibition the inhibitor decreases the maximum velocity without changing the MICHAELIS constant.

A third and less common type of inhibition is that in which both the maximum velocity and the MICHAELIS constant are reduced to a similar extent, so that there is no change in the ratio K_m/V as evaluated from the plots of Table 23. This type of inhibition has been termed 'uncompetitive' and is illustrated by the action of azide on the oxidized form of cytochrome oxidase¹⁹. The appropriate equation is based on the assumption that the inhibitor combines only with the enzyme-substrate compound:

$$v = \frac{V[S]}{K_m + [S] (1 + [I]/K_i)} \quad (5)$$

Plotting inhibition data. The different types of inhibition can be clearly differentiated by using any of the substrate plots of Table 23 and thus determining the effect of the inhibitor on the apparent K_m or V . Examples are shown in Figure 7 (page 383). K_i can be evaluated from the quantitative nature of this effect. To show that

Fig. 8 Inhibition data: plots of $1/v$ against $[I]$ ^{3,15}

Each line represents data for a series of inhibitor concentrations $[I]$ but at different substrate concentrations $[S]$.

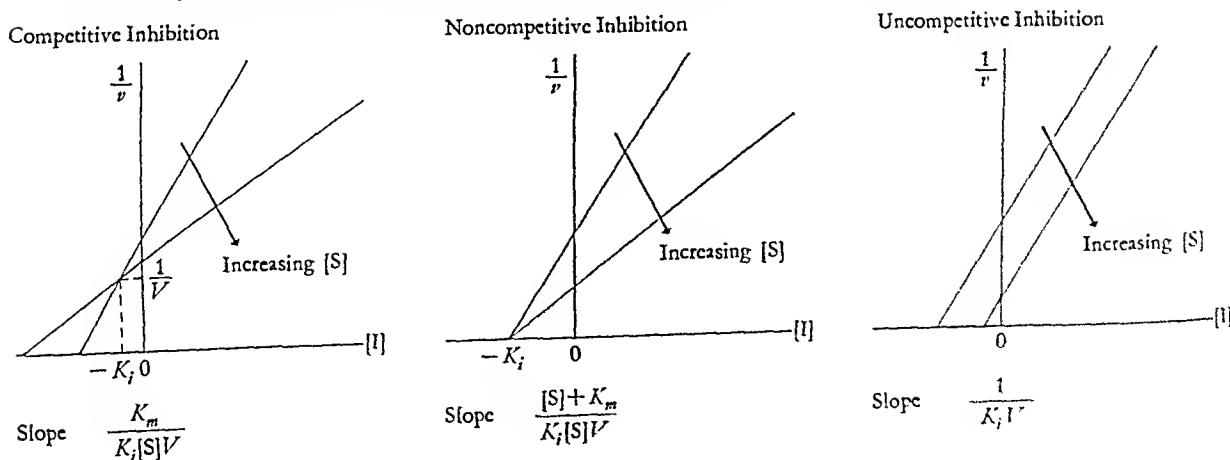


Table 24 (continued) Classification and numbering of enzymes

<p>2. Transferases (continued)</p> <p>2.4 Glycosyltransferases</p> <p>2.4.1 Hexosyltransferases</p> <p>2.4.2 Pentosyltransferases</p> <p>2.5 Transferring alkyl or related groups</p> <p>2.6 Transferring nitrogenous groups</p> <p>2.6.1 Aminotransferases</p> <p>2.6.3 Oximinotransferases</p> <p>2.7 Transferring phosphorus-containing groups</p> <p>2.7.1 Phosphotransferases with an alcohol group as acceptor</p> <p>2.7.2 Phosphotransferases with a carboxyl group as acceptor</p> <p>2.7.3 Phosphotransferases with a nitrogenous group as acceptor</p> <p>2.7.4 Phosphotransferases with a phospho group as acceptor</p> <p>2.7.5 Phosphotransferases, apparently intramolecular</p> <p>2.7.6 Pyrophosphotransferases</p> <p>2.7.7 Nucleotidyltransferases</p> <p>2.7.8 Transferases for other substituted phospho groups</p> <p>2.8 Transferring sulphur-containing groups</p> <p>2.8.1 Sulphurtransferases</p> <p>2.8.2 Sulphotransferases</p> <p>2.8.3 CoA-transferases</p> <p>3. Hydrolases</p> <p>3.1 Acting on ester bonds</p> <p>3.1.1 Carboxylic ester hydrolases</p> <p>3.1.2 Thiolester hydrolases</p> <p>3.1.3 Phosphoric monoester hydrolases</p> <p>3.1.4 Phosphoric diester hydrolases</p> <p>3.1.5 Triphosphoric monoester hydrolases</p> <p>3.1.6 Sulphuric ester hydrolases</p> <p>3.2 Acting on glycosyl compounds</p> <p>3.2.1 Glycoside hydrolases</p> <p>3.2.2 Hydrolysing <i>N</i>-glycosyl compounds</p> <p>3.2.3 Hydrolysing <i>S</i>-glycosyl compounds</p> <p>3.3 Acting on ether bonds</p> <p>3.3.1 Thioether hydrolases</p> <p>3.4 Acting on peptide bonds (peptide hydrolases)</p> <p>3.4.1 α-Amino-acyl-peptide hydrolases</p> <p>3.4.2 Peptidyl-amino-acid hydrolases</p> <p>3.4.3 Dipeptide hydrolases</p> <p>3.4.4 Peptidyl-peptide hydrolases</p> <p>3.5 Acting on C–N bonds other than peptide bonds</p> <p>3.5.1 In linear amides</p> <p>3.5.2 In cyclic amides</p> <p>3.5.3 In linear amidines</p> <p>3.5.4 In cyclic amidines</p> <p>3.5.5 In cyanides</p> <p>3.5.99 In other compounds</p> <p>3.6 Acting on acid-anhydride bonds</p> <p>3.6.1 In phosphoryl-containing anhydrides</p> <p>3.7 Acting on C–C bonds</p> <p>3.7.1 In ketonic substances</p>	<p>3.8 Acting on halide bonds</p> <p>3.8.1 In <i>C</i>-halide compounds</p> <p>3.8.2 In <i>P</i>-halide compounds</p> <p>3.9 Acting on P–N bonds</p> <p>4. Lyases</p> <p>4.1 Carbon-carbon lyases</p> <p>4.1.1 Carboxy-lyases</p> <p>4.1.2 Aldehyde-lyases</p> <p>4.1.3 Ketoacid-lyases</p> <p>4.2 Carbon-oxygen lyases</p> <p>4.2.1 Hydro-lyases</p> <p>4.2.99 Other carbon-oxygen lyases</p> <p>4.3 Carbon-nitrogen lyases</p> <p>4.3.1 Ammonia-lyases</p> <p>4.3.2 Amidine-lyases</p> <p>4.4 Carbon-sulphur lyases</p> <p>4.5 Carbon-halide lyases</p> <p>4.99 Other lyases</p> <p>5. Isomerases</p> <p>5.1 Racemases and epimerases</p> <p>5.1.1 Acting on amino acids and derivatives</p> <p>5.1.2 Acting on hydroxy acids and derivatives</p> <p>5.1.3 Acting on carbohydrates and derivatives</p> <p>5.1.99 Acting on other compounds</p> <p>5.2 Cis-trans isomerases</p> <p>5.3 Intramolecular oxidoreductases</p> <p>5.3.1 Intereconverting aldoses and ketoses</p> <p>5.3.2 Interconverting keto and enol groups</p> <p>5.3.3 Transposing C=C bonds</p> <p>5.4 Intramolecular transferases</p> <p>5.4.1 Transferring acyl groups</p> <p>5.4.2 Transferring phosphoryl groups</p> <p>5.4.99 Transferring other groups</p> <p>5.5 Intramolecular lyases</p> <p>5.99 Other isomerases</p> <p>6. Ligases</p> <p>6.1 Forming C–O bonds</p> <p>6.1.1 Amino acid-RNA ligases</p> <p>6.2 Forming C–S bonds</p> <p>6.2.1 Acid-thiol ligases</p> <p>6.3 Forming C–N bonds</p> <p>6.3.1 Acid-ammonia ligases (amide synthetases)</p> <p>6.3.2 Acid-amino-acid ligases (peptide synthetases)</p> <p>6.3.3 Cyclo-ligases</p> <p>6.3.4 Other C–N ligases</p> <p>6.3.5 C–N ligases with glutamine as N donor</p> <p>6.4 Forming C–C bonds</p>
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¹ International Union of Biochemistry, *Report of the Commission on Enzymes*, Pergamon Press, Oxford, 1961; International Union of Biochemistry, *Nomenclature, Recommendations* 1964, Elsevier, Amsterdam, 1965.

Cell metabolism

The metabolism of the whole body is the result of the metabolic activities of the component tissues. Within the last 40 years methods have become available for the study of the metabolic activities of isolated tissues and organs. In particular, measurements have been made of the rate of respiration and lactic acid fermentation of many types of cells and tissues. A few representative figures for animal tissues are given in Tables 1 and 2.

Table 1 Rate of respiration (Q_{O_2}) of animal tissues*

Representative values, measured on isolated tissues, usually slices suspended in glucose-saline medium at 38–40°C. Unless otherwise stated the data refer to rat tissues. For further data see the literature†.

Tissue	Q_{O_2}	Tissue	Q_{O_2}
Kidney cortex ..	-25	Rous sarcoma (chicken)	-5
Kidney medulla (guinea-pig) . . .	-8	FLENNER's carcinoma . .	-8
Liver	-13	Erythrocytes	-0.6
Brain cortex . . .	-12	Leucocytes	-9
Brain, white matter	-6	Thrombocytes	-7
Retina	-30	Bone marrow, red . . .	-10
Spleen	-12	Adipose tissue** . . .	-0.5
Lung	-8	Connective tissue (renal capsule, goat) . . .	-1
Submaxillary gland	-12	Cartilage (costal) . . .	-0.5
Pancreas	-4	Skin (newborn rat) . .	-1
Intestinal mucosa	-12	Striated muscle . . .	-
Colonic mucosa . .	-10	- diaphragm	-7
Adrenal gland . . .	-10	- gastrocnemius . . .	-3
Pituitary gland . .	-12	- breast muscle (pigeon, minced) . . .	-40
Thymus gland . . .	-5	Smooth muscle (gizzard, pigeon)	-4
Thyroid (guinea-pig)	-8	Cardiac muscle (sheep, minced) . . .	-18
Tetanus	-10		
JENSEN's sarcoma	-11		

* The magnitude of respiration and fermentation is commonly expressed by the 'metabolic quotients', defined as follows:

$$Q_{O_2} = \frac{\text{microlitres of } O_2 \text{ used}}{\text{milligrammes dry weight} \times \text{hours}}$$

$$Q_{CO_2} = \frac{\text{microlitres of } CO_2 \text{ used or produced}}{\text{milligrammes dry weight} \times \text{hours}}$$

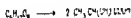
$$Q_{\text{lactic acid or } Q_L} = \frac{\text{microlitres of lactic acid formed}}{\text{milligrammes dry weight} \times \text{hours}}$$

The disappearance of a substance is usually indicated by a negative sign, the formation by a positive sign. Anaerobic and aerobic conditions are denoted by the superscripts N_2 and O_2 e.g. $Q_{O_2}^{aer}$, $Q_{N_2}^{ana}$.

So far little more than a beginning has been made in the biochemical analysis of disease. The knowledge summarized in the following pages represents a foundation upon which molecular pathology will develop.

Energy metabolism

The need for energy springs from the fact that living matter is a thermodynamically unstable system that cannot be maintained unless energy is continuously added. Moreover, living matter is constantly engaged in performing various kinds of work, such as movement, chemical syntheses and transporting substances against concentration gradients. Activities of this kind cannot take place unless there is a supply of energy. Warm-blooded organisms need energy also to maintain the body temperature.



Micro-organisms possess many forms of fermentation, among which the most important is the alcoholic fermentation

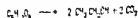


Table 2 Rate of anaerobic lactic acid fermentation ($Q_{\text{lactic acid}}^{N_2}$) in animal tissues*

Representative values, measured on isolated tissues, usually slices suspended in glucose-saline medium at 38–40°C. Unless otherwise stated the data refer to rat tissues. For further data see the literature[†].

Tissue	$Q_{\text{lactic acid}}^{N_2}$	Tissue	$Q_{\text{lactic acid}}^{N_2}$
Kidney cortex	3	Testis	8
Kidney medulla (guinea-pig)	28	JENSEN's sarcoma	32
Liver	3	Rous sarcoma (chicken) ..	30
Brain cortex	18	FLENNER's carcinoma ...	30
Retina	88	Erythrocytes	0.35
Retina (pigeon)	180	Leucocytes (polymorpho-nuclear, rabbit)	22
Spleen	8	Leucocytes (mono-nuclear, rabbit)	22
Lung (rat embryo) ...	10	Thrombocytes	26
Submaxillary gland ...	5	Bone marrow, red	21
Pancreas (rabbit)	3.5	Adipose tissue**	0.7
Intestinal mucosa	14	Cartilage (costal)	1.5
Adrenal gland	4	Skin (newborn rat)	7
Pituitary gland	13	Embryo	12
Thymus gland	8		

* See footnote * to Table 1, page 387.

** Calculated for dry weight less ether-soluble matter.

[†] KREBS and JOHNSON, *Tab. biol. (Amst.)*, 19, 100 (1948); ALBRITTON, E.C. (Ed.), *Standard Values in Nutrition and Metabolism*, Saunders, Philadelphia, 1954.

There are wide variations in the metabolic activities of different materials. The highest rates of respiration and fermentation found among micro-organisms. *Azotobacter*, for example, at 30°C can give Q_{O_2} values of over 8000, and rates of 100–200 are common among bacteria. Anaerobic fermentation rates in micro-organisms reach figures up to 400. The maximum rate of lactic acid production in muscle can probably reach $Q_{\text{lactic acid}}^{N_2}$ values of well over 100 for short periods. Avian retina gives the highest continuous rate of lactic acid production among animal tissues ($Q_{\text{lactic acid}}^{N_2} = 180$ in pigeon retina).

Low metabolic rates are generally found in tissues of relatively low physiological activity. This is true for resting glands or muscle and in particular for tissues whose function, like that of connective tissue or bone, is largely structural or, like that of adipose tissue, is concerned with the storage of metabolically inert material.

The rates of respiration and fermentation increase with temperature, like the majority of other chemical reactions. At a critical temperature – in the case of warm-blooded animals at about 40°C in the case of cold-blooded animals somewhat below this temperature – a further rise in temperature reduces metabolism. In exceptional cases, those of the thermophilic bacteria, the critical temperature may be as high as 80°C.

Among the factors which affect energy production in the intact warm-blooded animal, body size has long been recognized as being of major importance. The differences in the oxygen consumption of intact animals of different size are not exactly reflected in the rates of respiration of individual tissues. In general, the tissues of larger species have a somewhat lower metabolism than the tissues of smaller species, but the differences between the Q_{O_2} values of, for example, brain, kidney, liver, spleen and lung of different species are relatively small. The characteristic differences in the basal metabolic rate of animals of different size appear to be due mainly to differences in the resting metabolism of the musculature.

Metabolism – Energy-Supplying Reactions

Energy-supplying reactions

compound or of a series of closely related compounds. The basic details of these enzymes are described on pages 405–419.

Intermediary stages of carbohydrate degradation

Hexoses formed by digestion in the intestinal tract are absorbed and reach the various tissues through the blood circulation. The main reaction by which hexoses are degraded is the anaerobic

Digestion is brought about by the combined action of many specific enzymes each dealing with the hydrolysis of one com-

Table 3 Intermediary reactions of lactic acid fermentation (glycolysis) in animal tissues (for formulae of intermediates see Figure 1). These reactions occur in all animal tissues and in many micro-organisms.

No	Intermediary reactions	Enzyme catalysing the reaction*
1	glucose + adenosine triphosphate (ATP) → glucose 6-phosphate + adenosine diphosphate (ADP)	Hexokinase
2	glucose 6-phosphate → fructose 6-phosphate	Glucosephosphate isomerase
3	fructose 6-phosphate + ATP → fructose 1,6-diphosphate + ADP	Phosphofructokinase
4	fructose 1,6-diphosphate → dihydroxyacetone phosphate + 3-phosphoglyceraldehyde	Fructose diphosphate aldolase
5	dihydroxyacetone phosphate → 3-phosphoglyceraldehyde	Triosephosphate isomerase
6	2 [3-phosphoglyceraldehyde + diphosphopyridine nucleotide (NAD) + phosphate] → 2 1,3-diphosphoglyceric acid + NADH ₂	Glyceraldehyde phosphate dehydrogenase
7	2 [1,3-diphosphoglyceric acid + ADP] → 2 3-phosphoglyceric acid + ATP	Phosphoglycerate kinase
8	2 [3-phosphoglyceric acid] → 2-phosphoglyceric acid	Phosphoglycerate phosphomutase
9	2 [2-phosphoglyceric acid] → phosphopyruvic acid + H ₂ O	Phosphopyruvate hydratase
10	2 [phosphopyruvic acid + ADP] → 2 pyruvic acid + ATP	Pyruvate kinase
11	2 [pyruvic acid + NADH ₂] → 2 lactic acid + NAD	Lactate dehydrogenase
	Balance glucose + 2 ADP + 2 phosphate → 2 lactic acid + 2 ATP + 2 H ₂ O	

* On enzyme nomenclature see page 352

Fig. 1 The intermediates of glycolysis formed from glucose

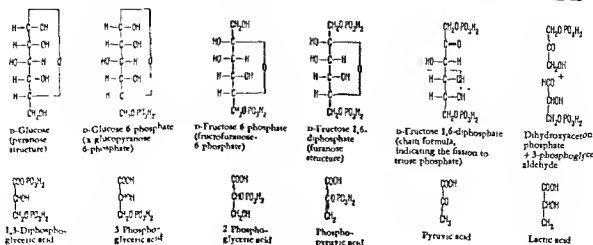


Table 4 Ancillary reactions of lactic acid fermentation in animal tissues

No.	Intermediary reactions		Enzyme catalysing the reaction
1	glycogen _n + phosphate	\rightleftharpoons glucose 1-phosphate + glycogen _{n-1}	α -Glucan phosphorylase
2	glucose 1-phosphate	\rightleftharpoons glucose 6-phosphate	Phosphoglucomutase
3	fructose + ATP	\rightarrow fructose 6-phosphate + ADP	Hexokinase*
4	galactose + ATP	\rightarrow galactose 1-phosphate + ADP	Galactokinase ²
5	galactose 1-phosphate + uridine diphosphoglucose	\rightleftharpoons glucose 1-phosphate + uridine diphosphogalactose	Hexose 1-phosphate uridylyl-transferase ³
6	uridine diphosphogalactose	\rightleftharpoons uridine diphosphoglucose	UDPglucose epimerase ⁴
7	uridine diphosphoglucose + pyrophosphate	\rightleftharpoons uridine triphosphate (UTP) + glucose 1-phosphate	UDPG pyrophosphorylase ⁵
8	fructose + ATP	\rightarrow fructose 1-phosphate + ADP	Ketohexokinase ⁶
9	fructose 1-phosphate	\rightleftharpoons dihydroxyacetone phosphate + glyceraldehyde	Ketose 1-phosphate aldolase ⁷
10	D-glyceraldehyde + ATP	\rightarrow glyceraldehyde 3-phosphate + ADP	Triokinase ⁸

* Hexokinase reacts similarly with many other hexoses, e.g., mannose, 2-deoxyglucose¹.

References

¹ SOLS and CRANE, *J. biol. Chem.*, **240**, 581 (1954).

² TRUCCO et al., *Arch. Biochem.*, **18**, 137 (1948).

³ KALCKAR et al., *Nature*, **172**, 1038 (1953); SMITH and MILLS, *Biochim. biophys. Acta (Amst.)*, **13**, 386 (1954).

⁴ LELOIR, L.F., *Arch. Biochem.*, **33**, 186 (1951); KALCKAR, H.M., *Advan. E. zymol.*, **20**, 111 (1958).

⁵ MUNCH-PETERSEN et al., *Nature*, **172**, 1036 (1953); ISSELBACHER, K.J., *J. biol. Chem.*, **232**, 429 (1958).

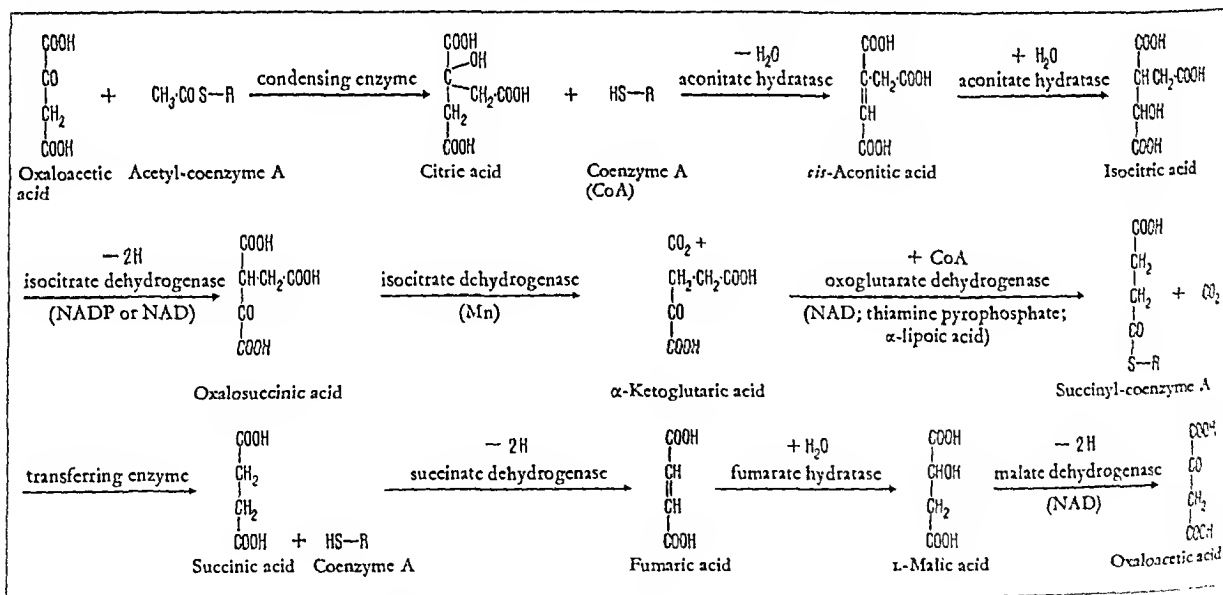
⁶ HERS and KUSAKA, *Biochim. biophys. Acta (Amst.)*, **11**, 427 (1953); PARK et al., *J. biol. Chem.*, **227**, 231 (1957).

⁷ PEANASKY and LARDY, *J. biol. Chem.*, **233**, 365 and 371 (1958).

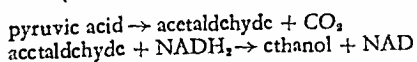
⁸ BERGMAYER et al., *Biochem. Z.*, **333**, 471 (1961).

Fig. 2 The individual stages of the tricarboxylic acid cycle

The names of the enzymes are given above the arrows, those of the coenzymes required below the arrows.

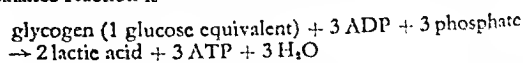


Anaerobic lactic acid fermentation (glycolysis). The intermediary reactions of the lactic acid fermentation are given in Table 3. The changes of the carbon skeleton are summarized in Figure 1. The alcoholic fermentation of yeasts, moulds, other micro-organisms and plants follows essentially the same pathway except that reaction 11 (Table 3) is replaced by the following two reactions:



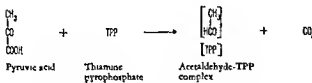
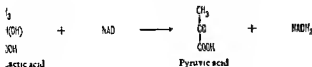
... of the alcoholic fermentation (reactions 1-10)

Reactions related to the lactic acid fermentation are shown in Table 4. Some of these reactions are concerned with the fermentation of other starting materials such as glycogen, fructose or galactose. When glycogen (or starch) is the starting material the balance reaction is

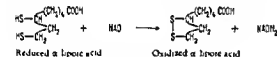
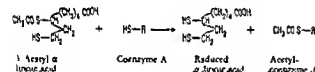
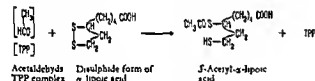


Oxidation of carbohydrate. As a rule, sugars are not oxidized as

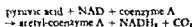
Lactic acid is first converted into acetyl-coenzyme A via pyruvic acid. The intermediary stages are assumed to be as follows:



In the succeeding reaction the aldehyde-TPP complex reacts with

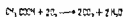


The sum of the last four reactions is



Analogous reactions probably occur whenever α-ketonic acids are oxidized. α-Ketonic acids arise in particular from α-amino acids. α-Ketoglutarate is also formed during the tricarboxylic acid cycle.

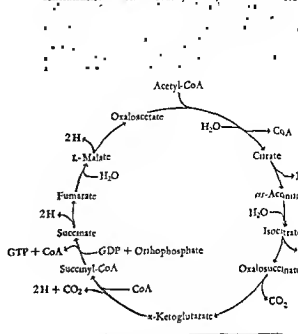
Acetyl-coenzyme A is oxidized to completion by the tricarboxylic acid cycle (also referred to in the literature as the 'citric acid cycle' or 'Krebs cycle'). This cycle is initiated by a condensation of acetyl-coenzyme A and oxaloacetate leading to citrate. Citrate undergoes a series of reactions that, on balance, are oxidative and in which other tricarboxylic acids and dicarboxylic acids arise. They lead eventually to the regeneration of oxaloacetate, which thus becomes available for another turn of the cycle. This means that oxaloacetate reacts after the manner of a catalyst. The hydrogen atoms arising in the course of the cycle react ultimately with molecular oxygen to form water, and the overall effect of one turn of the cycle is therefore



The component reactions of the cycle are given in Figure 2. The cycle itself is shown diagrammatically in Figure 3.

Fig 3 The tricarboxylic acid cycle

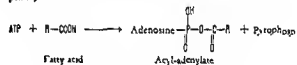
Substances entering the cycle (coenzyme A, H₂O) after the in condensation of 1 molecule of acetyl-coenzyme A and 1 molecule



Oxidative degradation of fat (for references see page 393)

Fats are not oxidized in the ester form in which they are posited in tissues and present in foods. Prior to oxidation, they are hydrolysed to free fatty acids and glycerol, a reaction catalysed by lipases or other ester hydrolases.

The stages of the reaction have been identified. The first leads to formation of an adenylyl fatty acid (acyl-adenosine monophosphate):



The second is a transfer of the acyl group from adenylyl acyl-coenzyme A:

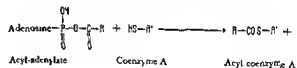
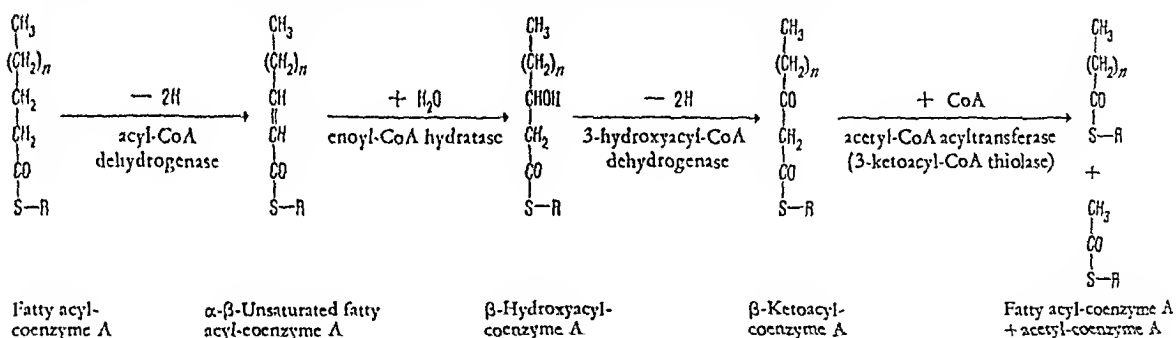


Fig. 4 β -Oxidation of fatty acids

On enzyme nomenclature see page 382. Acyl-CoA-dehydrogenase is a flavoprotein, 3-hydroxyacyl-CoA-dehydrogenase requires NAD. All four reactions are reversible. The β -hydroxyacyl-coenzyme A compounds are optically active and belong to the L-series, in contrast to the free β -hydroxybutyrate in blood and urine which belongs to the D-series. The latter arises by reduction of free acetoacetate⁴.

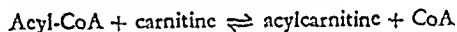


less than four carbon atoms. In the case of chains with even numbers of carbon atoms the last fragment is acetyl-coenzyme A, in the case of those with uneven numbers it is propionyl-coenzyme A.

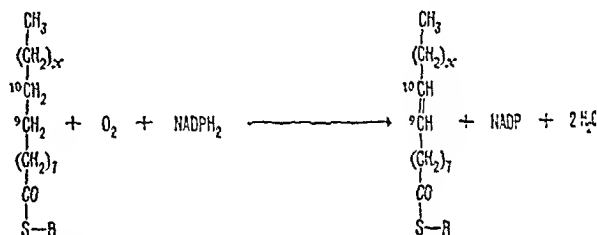
The great majority of naturally occurring fatty acids contain an even number of carbon atoms and therefore yield acetyl-coenzyme A as the only product. The propionyl-coenzyme A formed from uneven chains is known to enter a CO_2 -fixation reaction leading to succinic acid (see below).

The sequence of reactions by which fatty acids are oxidized has been referred to as the 'fatty-acid cycle'. It is not a cycle in the strict sense since the starting material is not regenerated by a full turn of the 'cycle'. What happens is a periodic repetition of the same *types* of reaction, but not of the same reactions. This is shown diagrammatically in Figure 5, from which it can be seen that the mechanism is a 'spiral' rather than a 'cycle'.

Carnitine (page 491) stimulates oxidation of fatty acids by promoting their transport from cytoplasm^{1,2} to mitochondria through the formation of carnityl esters:

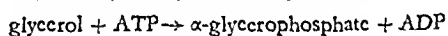


Unsaturated fatty acids are formed by desaturation of the coenzyme A esters of saturated fatty acids. This involves a coupled reaction in which both molecular oxygen and NADPH_2 are required⁵:



Unsaturated fatty acids are also degraded by β -oxidation^{1,2}. The double bond necessitates two additional enzymes, an isomerase that transposes it and converts it from *cis* to *trans* configuration, and an epimerase that converts the β -hydroxyacyl-coenzyme A formed by addition of H_2O to the bond from the D- to the L-configuration. The latter is then degraded as shown in Figure 4.

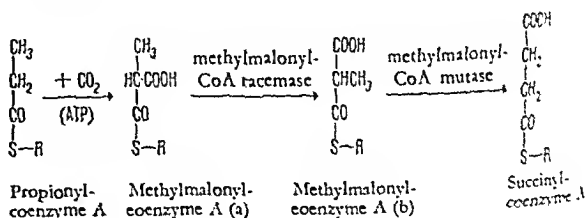
Glycerol, the second constituent of neutral fats, is converted in liver primarily to α -glycerophosphate:



Alternatively, glycerol may be dehydrogenated to D-glyceraldehyde, which can yield glyceraldehyde 3-phosphate, or 2-phosphoglyceric acid via D-glycerate⁶.

The triose phosphate formed from glycerol subsequently joins the reactions of triose phosphate arising from sugars.

Formation of succinic acid from propionyl-coenzyme A. As already mentioned, the propionyl-coenzyme A formed from fatty acids with uneven carbon chains yields succinic acid. This involves a CO_2 -fixation reaction discovered by OCHOA et al.⁷ followed by racemization and rearrangement of methylmalonyl-coenzyme A⁸ as follows⁹:



Hydrolysis of succinyl-coenzyme A then gives succinic acid.

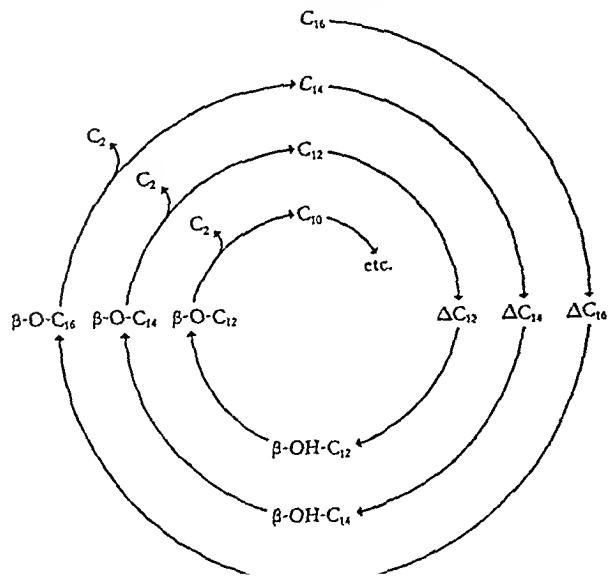
Terminal oxidation of fat. The degradation reactions of fat so far considered bring about an incomplete oxidation of fatty acids and glycerol. The main product of this incomplete oxidation is acetic acid in the form of acetyl-coenzyme A. The only other product is succinic acid, which arises from the three terminal carbon atoms of the fatty-acid chain with odd numbers of carbon atoms. Since fatty acids with odd numbers of carbon atoms are uncommon in nature the total amount of succinate arising from fat is normally very small. Such fatty acids are uncommon because fatty-acid chains are usually synthesized from 2-carbon units.

Acetyl-coenzyme A and succinate are oxidized to completion by the reactions of the tricarboxylic acid cycle described on pages 390 and 391.

Fig. 5 Diagram of the 'spiral' of fatty-acid oxidation

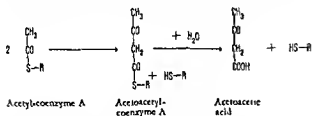
$\text{C}_{16}, \text{C}_{14}$, etc. = fatty acyl-coenzyme A
 $\Delta\text{C}_{16}, \Delta\text{C}_{14}$, etc. = unsaturated fatty acyl-coenzyme A
 $\beta\text{-OH-C}_{16}, \beta\text{-OH-C}_{14}$, etc. = β -hydroxyacyl-coenzyme A
 $\beta\text{-O-C}_{16}, \beta\text{-O-C}_{14}$, etc. = β -ketoacyl-coenzyme A
 C_2 = acetyl-coenzyme A

The subscripts indicate the length of the carbon chain

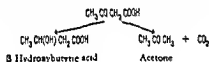


Ketosis. In ketosis due to starvation or diabetes or other causes, the 'ketone bodies', viz. acetoacetate ($\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{COOH}$),

acetyl-coenzyme A condense in pairs to form acetoacetyl-coenzyme A which undergoes hydrolysis to free acetoacetate and coenzyme A (in liver free acetoacetate is not readily utilized).



Acetoacetate is the primary ketone body. β -Hydroxybutyrate is formed from it by reduction, acetone by decarboxylation. The latter reaction is mainly nonenzymic, and is due to the inherent instability of acetoacetate.



The above are the stages of ketone body formation.

It follows that all substances which can form acetyl-coenzyme A

This is analogous to the reaction initiating the degradation of fatty acids (page 391) and may involve the same type of intermediary stages, i.e., the formation of acetoacetyl-adenylate

References

KREBS, H. A. *Arch. intern. Med.*, 107, 51 (1961); WIELAND and LEFFLER, *Biochem. Z.* 220 104 (1961)

Intermediary stages of the degradation of amino acids

General degradation reactions. Some degradation reactions are common to all or several amino acids. These are (a) oxidative desamination, (b) transamination, (c) nonoxidative decarboxylation.

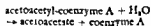
Oxidative desamination. The general reaction scheme of oxidative desamination is as follows:



Liver and kidney contain enzymes that catalyze this reaction.

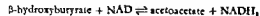
Ancillary reactions of fatty acid degradation. Some ancillary degradation reactions of fatty acids are the following:

(a) Acetoacetyl-CoA-hydrolase liberates free acetoacetate from the coenzyme A derivative



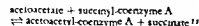
This reaction is assumed to play a role in the appearance of the ketone bodies in blood and tissues in ketosis.²⁸

(b) 3-Hydroxybutyrate dehydrogenase catalyses the reversible interconversion of acetoacetate and β -hydroxybutyrate

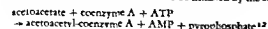


and is responsible for the formation and removal of β -hydroxybutyrate

(c) An enzyme transferring coenzyme A reversibly between acetoacetate and succinate (3 ketoacid CoA-transferase) may initiate the breakdown of free acetoacetate



(d) Acetoacetate breakdown can also be initiated by the reaction



This enzyme differs from all the other enzymes in that it

Transamination. Transamination is a reversible reaction between amino and α -keto acids leading to the exchange of the amino and ketonic groups. An example is the following:

Table 5 Some transamination reactions in animal tissues¹

Reactions			Remarks
α -ketoglutarate + L- α -amino acid	\rightleftharpoons	L-glutamate + α -ketonic acid	Most α -amino acids can react in this way in liver and many other tissues
α -ketoglutarate + L-ornithine	\rightleftharpoons	L-glutamate + L-glutamic γ -semialdehyde	Involves transfer of ω -amino groups; occurs in liver ^{2,3}
glyoxylate + L-ornithine	\rightleftharpoons	glycine + L-glutamic γ -semialdehyde	
pyruvate + L-ornithine	\rightleftharpoons	L-alanine + L-glutamic γ -semialdehyde	
L-glutamine + α -keto- γ -guanidinovaleric acid	\rightleftharpoons	α -ketoglutarate + L-arginine + NH ₃	Occurs in liver ²
L-alanine + hydroxypyruvate	\rightleftharpoons	pyruvate + L-serine	Occurs in liver and kidney ⁴
α -ketoglutarate + γ -aminobutyrate	\rightleftharpoons	L-glutamate + succinic semialdehyde	Occurs in brain and liver ⁵
α -ketoglutarate + β -alanine	\rightleftharpoons	L-glutamate + malonic semialdehyde	Occurs in brain and liver ⁶

References

¹ For reviews see COHEN and SALLACH, in GREENBERG, D.M. (Ed.), *Metabolic Pathways*, vol. 2, Academic Press, New York, 1961, page 1; KREBS, H.A., in MUNRO and ALLISON (Eds.), *Mammalian Protein Metabolism*, vol. 1, Academic Press, New York, 1964, page 125; GUIRARD and SNELL, in FLORKIN and STOTZ (Eds.), *Comprehensive Biochemistry*, vol. 15, Elsevier, Amsterdam, 1964, page 138.

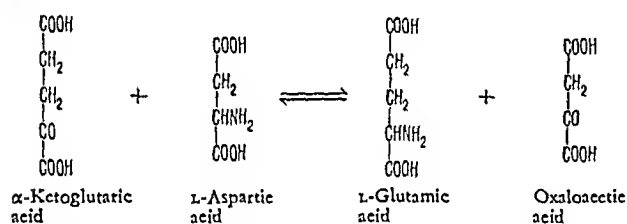
² MEISTER, A., *J. biol. Chem.*, 206, 587 (1954).

³ QUASTEL and WITTY, *Nature*, 167, 556 (1951).

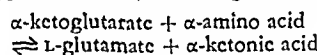
⁴ SALLACH, H.J., *J. biol. Chem.*, 223, 1101 (1956).

⁵ ROBERTS et al., *J. biol. Chem.*, 203, 195 (1953).

⁶ ROBERTS and BREGOFF, *J. biol. Chem.*, 201, 393 (1953).



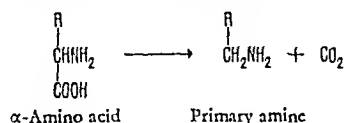
The majority of α -amino acids can replace aspartic acid in this type of reaction, according to the general scheme



but the rate of reaction is by far the highest when aspartic acid is the amino group donor. Transaminases occur in most animal tissues as well as in micro-organisms and plants. Several tissues contain special types of transaminases. Some of these tissues are listed in Table 5.

Transaminases readily diffuse from tissues into the blood plasma when the tissue has suffered damage. This is the basis of a clinical test, the rise of the plasma level of transaminase in cardiac infarction. Pyridoxal phosphate is a prosthetic group of transaminases.

Decarboxylation. Decarboxylation of amino acids proceeds according to the following general scheme:



Decarboxylases occur in animal tissues and in many micro-organisms, but not every amino acid can undergo decarboxylation. Reactions that have been recorded are listed in Table 6. The significance of some of the decarboxylations occurring in animal tissues lies in the supply of essential metabolites, e.g., of taurine (required for the synthesis of bile acids), of histamine and serotonin (required for the functional activities of nervous tissue) or of ethanolamine (required for the synthesis of cephalins, choline and acetylcholine). Pyridoxal phosphate (see page 474) is a coenzyme also in most decarboxylation reactions. A notable exception is the decarboxylation of histidine.

Degradation of individual amino acids¹

(for references see page 399)

L-Glutamic acid, L-aspartic acid, L-alanine. On oxidative deamination or transamination these three amino acids yield α -ketonic acids which also occur as intermediates in the metabolism of car-

Table 6 Decarboxylation of L-amino acids¹

Most of the bacterial reactions listed below occur in the micro-organisms of the intestinal tract, e.g., *Escherichia coli*, *Streptococcus faecalis*, *Clostridium* species

Amino acid	Amine formed	Occurrence of enzyme
Histidine	Histamine	Animal tissues, bacteria
Cysteic acid	Taurine	Liver
Glutamic acid	γ -Aminobutyric acid	Brain, bacteria
5-Hydroxytryptophan	5-Hydroxytryptamine (serotonin)	Animal tissues
3,4-Dihydroxyphenylalanine	3,4-Dihydroxyphenylethylamine	Animal tissues
Serine	Ethanolamine	Animal tissues ²
Lysine	Cadaverine	Bacteria
Ornithine	Putrescine	Bacteria
Tyrosine	Tyramine	Bacteria
Phenylalanine	Phenylethylamine	Bacteria
Aspartic acid	β -Alanine	Bacteria
α,ϵ -Diaminopimelic acid	Lysine	Bacteria ³

References

¹ For reviews see GUIRARD and SNELL, in FLORKIN and STOTZ (Eds.), *Comprehensive Biochemistry*, vol. 15, Elsevier, Amsterdam, 1964, page 138. KREBS, H.A., in MUNRO and ALLISON (Eds.), *Mammalian Protein Metabolism*, vol. 1, Academic Press, New York, 1964, page 125.

² ARNSTEIN, H.R.V., *Biochem. J.*, 48, 27 (1951).

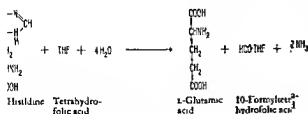
³ DEWEY and WORK, *Nature*, 169, 533 (1952).

bolhydrate; they are α -ketoglutarate, oxaloacetate and pyruvate respectively.

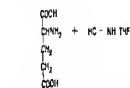
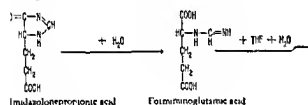
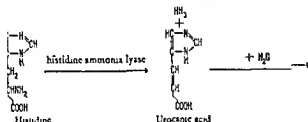
The degradation of the six amino acids L-histidine, L-arginine, L-citrulline, L-ornithine, L-proline and L-hydroxyproline leads in every case to glutamic acid and thence to α -ketoglutarate.

L-Histidine is converted to glutamic acid by an enzyme complex of liver tissue that includes tetrahydrofolic acid (THF) as a co-factor. The overall result of the action of this complex is an hydrolysis according to the following scheme:

(For references see page 399)



Six intermediate stages have been identified², of which the first the fission to ammonia and an unsaturated derivative of histidine.

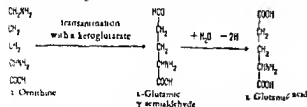


Formimino-THF is converted into 5,10-methylidene-THF and 10-formyl-THF. For these and further reactions see pages 436 and 437.

Oxidative deamination or transamination of histidine yields imidazolepyruvic acid², which may be further converted into imidazolelactic acid and imidazoleacetic acid.

A similar pathway of histidine degradation to glutamic acid has been shown in bacteria, although tetrahydrofolic acid does not appear to be involved.

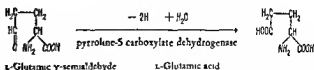
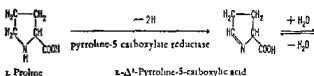
L-Citrulline and L-arginine are converted in liver tissue into ornithine by the reactions of the ornithine cycle (see pages 442 and 443). Ornithine is known to yield glutamic γ-semialdehyde by transamination (see page 394) and the semialdehyde can form glutamic acid by dehydrogenation.



D-Ornithine, under the influence of D-amino-acid oxidase, follows a different route, the primary step being the removal of the α-amino group.



L-Proline forms glutamic acid by the following three steps⁴, which include two dehydrogenations:



These reactions have been shown to occur in both liver and bacteria.

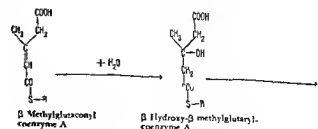
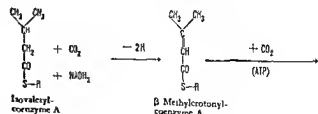
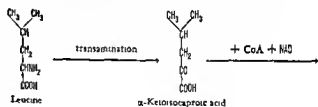
D-Proline reacts differently in mammalian liver or kidney and gives the same α-ketonic acid as D-ornithine. This is to be expected as the point of attack of D-amino-acid oxidase is always the α-carbon atom.

L-Hydroxyproline, γ-Hydroxyglutamic acid can be formed from L-proline by the action of L-proline-4-hydroxylase.

The degradation of the leucine and valine follows initially a com-

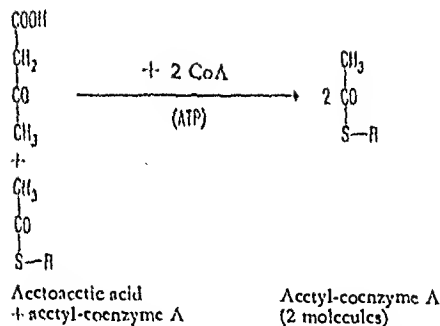
coenzyme A and propionyl-coenzyme A. As already mentioned (page 392), propionyl-coenzyme A eventually yields succinate.

Leucine yields three molecules of acetyl-coenzyme A. The intermediate stages are as follows⁴:

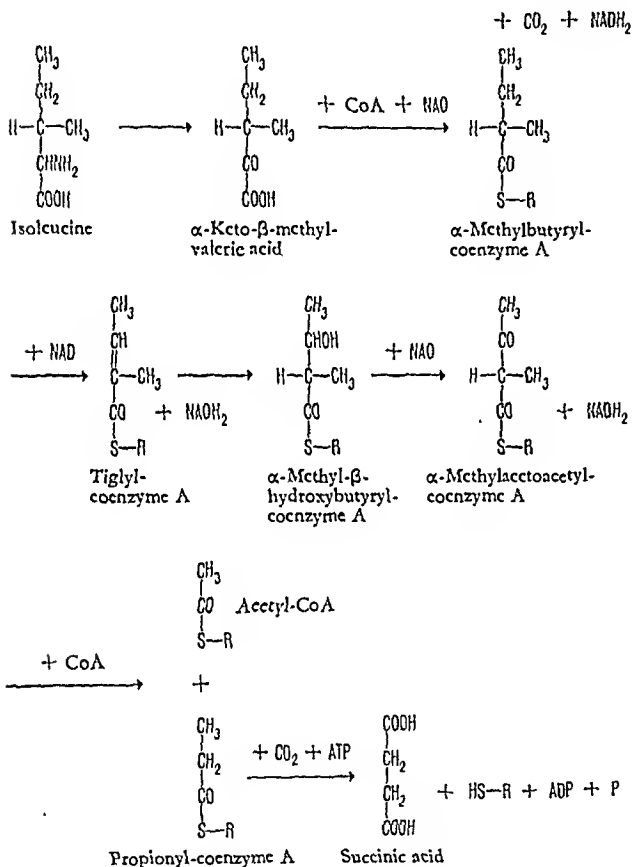


Metabolism - Energy-Supplying Reactions

(For references see page 399)

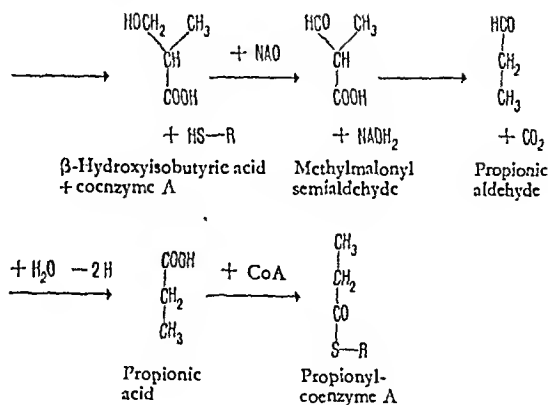
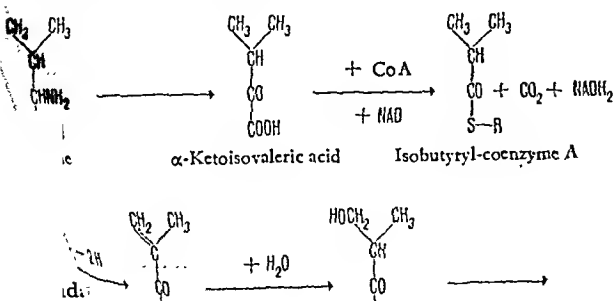


Isoleucine yields one molecule of acetyl-coenzyme A and one molecule of propionyl-coenzyme A:

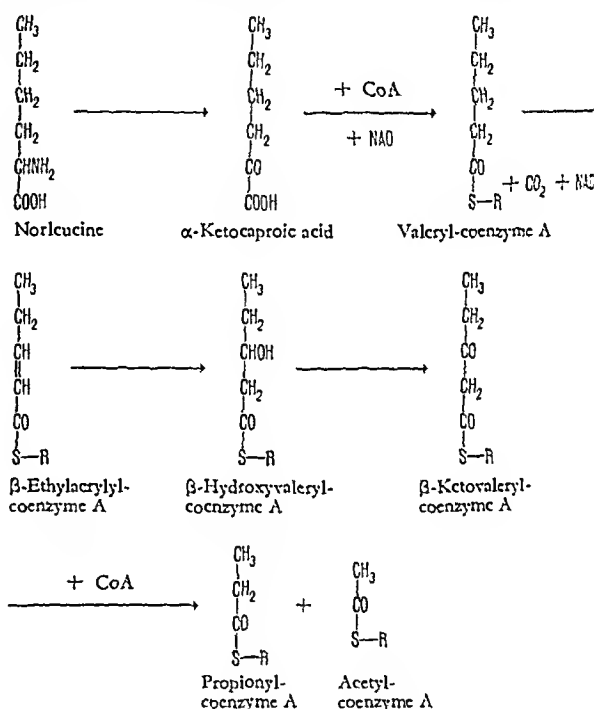


The mechanism of the last of these reactions is discussed on page 392.

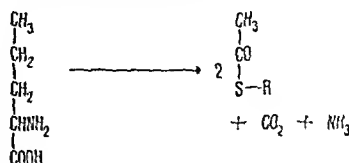
Valine is degraded by analogous reactions to the stage of β -hydroxyisobutyryl-coenzyme A. This compound is hydrolysed by a thiol ester hydrolase to yield β -hydroxyisobutyric acid, which is further metabolized as shown below:



Norleucine (which is not a protein constituent) has not been studied in detail, but by analogy it is expected to undergo the following sequence of reactions leading to propionyl-coenzyme A and acetyl-coenzyme A:



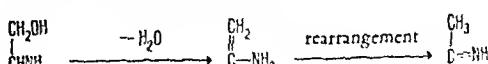
Norvaline, by the same types of reaction, forms two molecules of acetyl-coenzyme A:



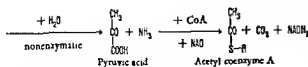
α -Aminobutyric acid by analogy forms propionyl-coenzyme A and thence succinate.

The *hydroxyamino acids* (serine, homoserine, threonine) and *glycine* react atypically in that the oxidative deamination is not the primary step.

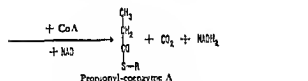
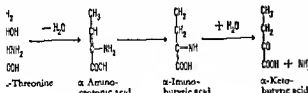
Serine yields anaerobically ammonia and pyruvic acid in animal tissues as well as in micro-organisms. The intermediate steps are assumed to be as follows:



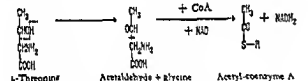
(For references see page 399)



1. *Threonine* (an intermediate in the metabolism of methionine) is known to undergo an analogous nonoxidative deamination on incubation with liver extracts, yielding α -ketobutyric acid and ammonia¹⁰:

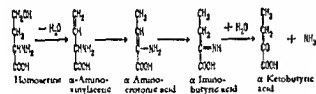


It may also be split by an aldolase to give acetaldehyde and glycine!!

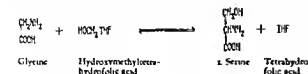


The acetaldehyde formed can be converted into acetyl-coenzyme A, whilst the glycine reacts as described later.

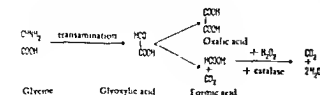
Homoserine (an intermediate in the metabolism of methionine) yields α -ketobutyric acid and ammonia by a nonoxidative deamination analogous to that of serine¹²



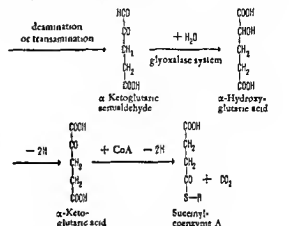
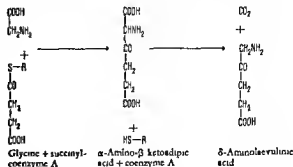
Glycine The pathway of degradation of glycine is not yet fully clarified. One route is the conversion into serine by an aldol condensation with hydroxymethyltetrahydrofolic acid.⁷³



only occurring in animal tissues.

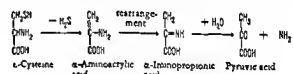


Another possible pathway of glycine degradation is initiated by the condensation with succinyl-coenzyme A¹⁸:



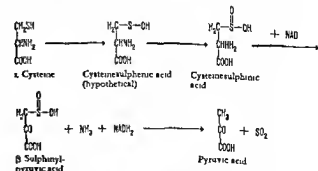
The reactions up to the stage of δ -aminolaevulinic acid have been firmly established but the pathway beyond δ -aminolaevulinic acid leading eventually to succinyl-coenzyme A is hypothetical and based on analogies.

L-Cysteine can be desulphurated, under the influence of the enzyme cysteine desulphhydrase, to yield pyruvate, NH_3 and H_2S ¹⁰. The intermediate stages have been formulated as follows:



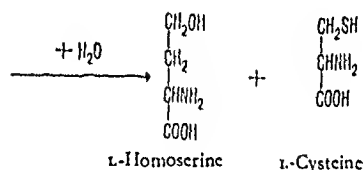
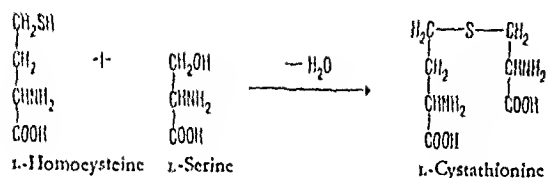
These reactions are closely analogous to those of serine

A more important metabolic route involves oxidation at the sulphur atom

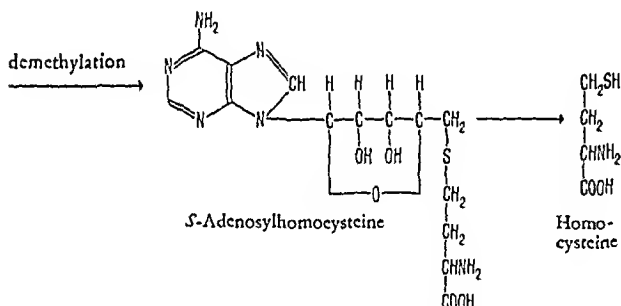
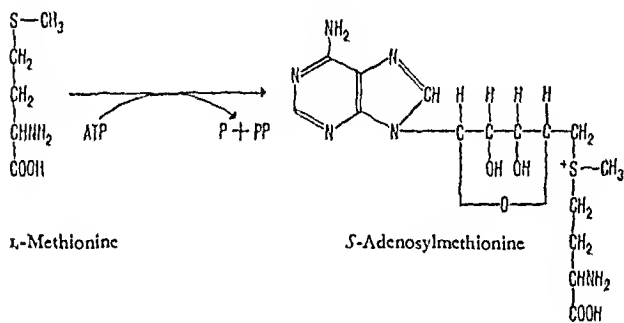


Cytine is converted in liver tissue into the same products as cysteine, it is assumed that it undergoes reduction to cysteine before it is degraded.

L-Homocysteine, an intermediate in methionine oxidation, undergoes a transsulphuration reaction with cystathionine as intermediate¹⁷. In this way the methionine sulphur becomes that of cysteine, the pathway of degradation of which is shown above.

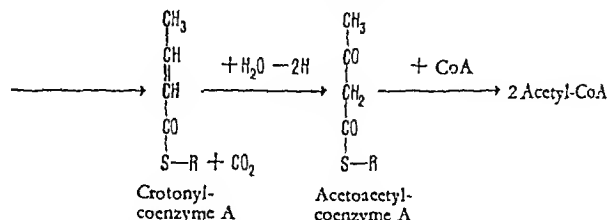
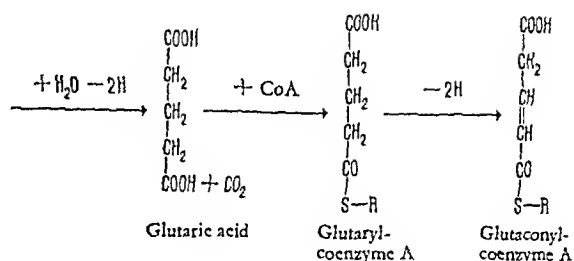
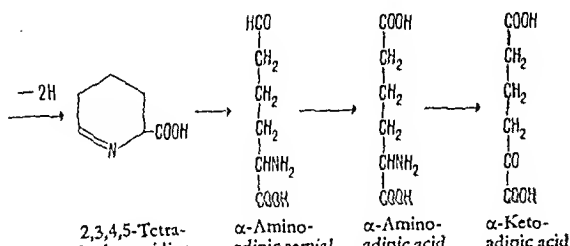
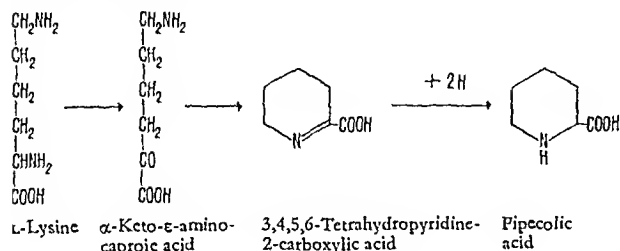


L-Methionine is first converted to an active form, a step requiring adenosine triphosphate (ATP)¹⁸. The product, S-adenosylmethionine, is a methyl group donor (in choline synthesis).

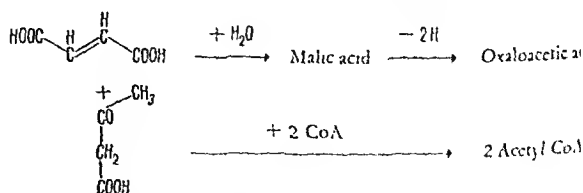
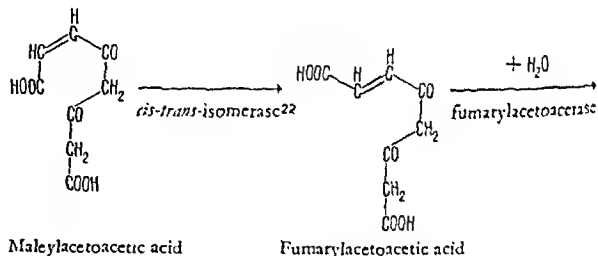
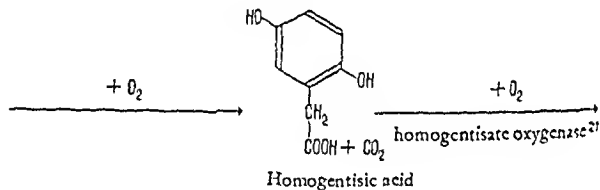
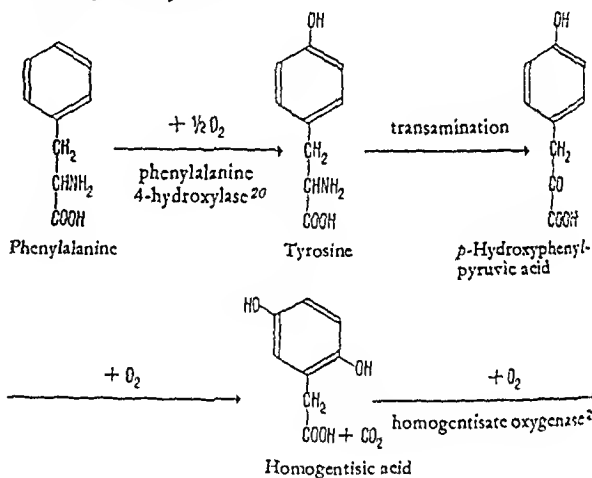


The fate of homocysteine has already been discussed.

L-Lysine. The following pathway of the degradation of lysine is essentially based on isotopic evidence and the isolation of most of the intermediates¹⁹:



Phenylalanine and tyrosine are degraded in animal tissues by the reactions shown in the following scheme. Several unusual enzymes are involved. The end-products as formulated are oxaloacetic acid and acetyl-coenzyme A:

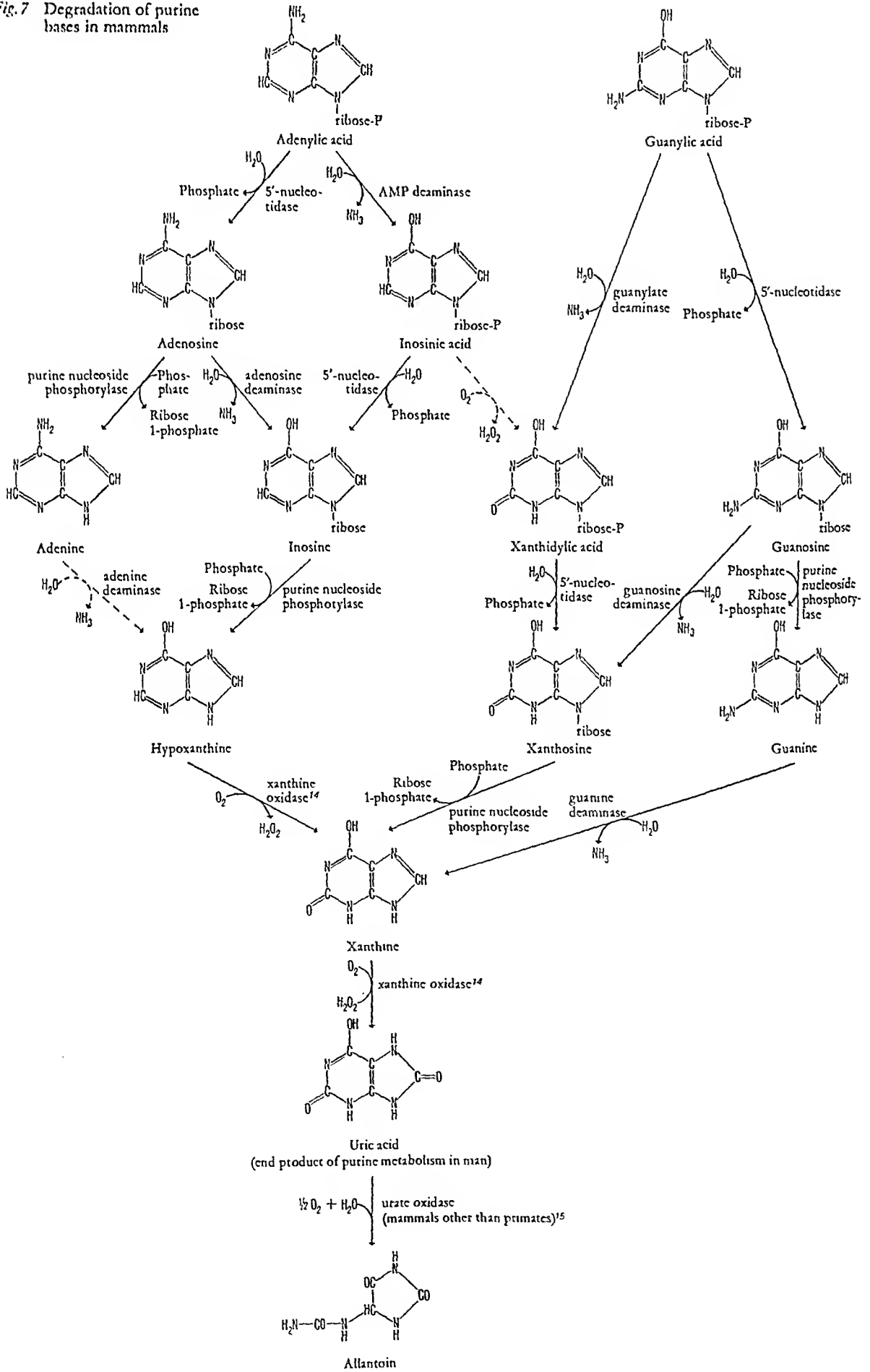


Fumaric acid + acetoacetic acid

On inborn errors of phenylalanine and tyrosine metabolism see pages 448-449.

Tryptophan is incompletely burned in man and in most animals. Products of incomplete oxidation appearing in the urine are indole 3-acetic acid, anthranilic acid, kynurenine, hydroxykynurenine, kynurenic acid and 8-hydroxykynurenine ('xanthurenic') acid. Tryptophan and 3-hydroxyanthranilic acid (but not anthranilic acid) can be converted into nicotinic acid in some animals, though only

Fig. 7 Degradation of purine bases in mammals



(continued from page 399)

Degradation of purine bases in man and mammals¹². The degradation

pathways depending on whether deamination and oxidation precede or do not precede the fission of the nucleotide or nucleoside. The end-product of purine degradation is the same, irrespective of the route. It is uric acid in man and other primates, and allantoin

relatively slow by broken arrows

Purine deaminases. Three types of enzyme are known - adenine deaminase, adenosine deaminase and AMP deaminase - that hydrolyse adenine, adenosine and AMP respectively to yield ammonia and the corresponding derivative of hypoxanthine. Of these, the occurrence of adenine deaminase in mammals is uncertain. Adenosine deaminase occurs in most tissues of higher animals. AMP deaminase occurs abundantly in striated muscle but is relatively weak in other tissues, including heart muscle¹³.

Three types of enzyme are known - guanine deaminase, guanosine deaminase, and guanylate deaminase - that hydrolyse guanine, guanosine and guanylate respectively to yield ammonia and the corresponding derivative of hypoxanthine.

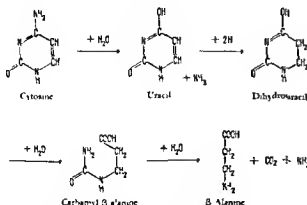
Purine oxidases. The oxidation of purines can occur at the zibotide level or at the free base level. The oxidation of inosinic acid to xanthine is a relatively slow reaction in mammals.

and in many tissues¹⁴

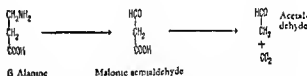
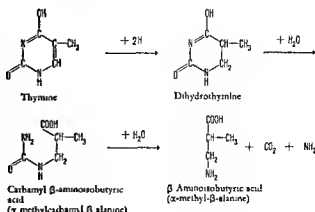
Urate oxidase oxidizes uric acid to allantoin¹⁵. It occurs in liver and kidney of mammals other than man and primates

Nucleotidases and purine nucleoside phosphorylases. The fission of nucleotides is hydrolytic, the products being nucleosides and inorganic phosphate. The fission of nucleosides in animals is phosphorylatic, the products being a purine base and ribose 1-phosphate. Micro-organisms also contain nucleoside hydrolases, but these have not so far been demonstrated in higher animals.

Degradation of pyrimidines. Cytosine and uracil are converted into β alanine by the liver through the following reaction sequence:



Thymine, by analogous reactions¹⁶, forms a methyl- β alanine in liver. Other pathways occur in bacteria¹⁷.



α -Methyl- β -alanine reacts in an analogous manner to give methylmalonic semialdehyde⁴, which can form propionaldehyde and subsequently succinic acid via propionyl-coenzyme A.

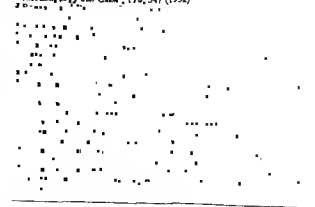
About 5-10% of humans excrete α -methyl- β -alanine in the urine in quantities up to 300 mg daily⁸. This is assumed to be an inborn error of metabolism. It is probably due to an abnormality in the enzymes responsible for the degradation of α -methyl- β -alanine⁶.

In cholesterol, only the side chain undergoes complete oxidation. A specific enzyme can cleave off the side chain, forming isocaproic acid and leaving the ring system in the form of pregnenolone⁷. Isocaproic acid in turn is broken down to propionic acid and acetyl-coenzyme A⁸. The ring system of cholesterol and the steroids is not oxidized to CO_2 ⁷.

Other cell constituents that are essentially not oxidized in the body to CO_2 are the *iron porphyrins* (see pages 359 sq.) derived from haemoglobin and cytochromes (these are excreted in the form of bile pigments and their derivatives, see page 362), and the *uronic acids* (see page 323) contained in mucins, in hyaluronic acid and in the chondroitin sulphate of cartilage and tendons.

References

1. RACKER, E. J. *Biol. Chem.*, 196, 347 (1952)



Degradation of the principal foodstuffs

consisting of several hexoses, glycerol, about twenty amino acids and a number of fatty acids – is incompletely burned. The products listed in Table 7, apart from carbon dioxide and water, are either acetic acid in the form of acetyl-coenzyme A or an intermediate of the tricarboxylic acid cycle, α -ketoglutarate, succinate, fumarate or oxaloacetate. Acetic acid constitutes the main product: two-thirds of the carbon of carbohydrate and glycerol, all the carbon of the common fatty acids and about half the carbon skeleton of amino acids yield acetyl-coenzyme A. α -Ketoglutarate arises from glutamic acid, histidine, arginine, citrulline, ornithine, proline and hydroxyproline; oxaloacetate from aspartate; fumarate from part of the benzene ring of tyrosine and phenylalanine; succinate from threonine, isoleucine, valine, methionine, α -aminobutyric acid, propionic acid and the three terminal carbon atoms of fatty acids with an odd number of carbon atoms.

The products of the first stage of the oxidative breakdown are completely oxidized in the second stage, the tricarboxylic acid cycle, which thus represents a common terminal pathway of oxidation shared by all foodstuffs. Almost two-thirds of the total energy released in the combustion of foodstuffs appears during the reactions of this cycle.

Any surplus oxaloacetate not required as a catalyst in the cycle can be decarboxylated to pyruvate, whence it is converted into acetyl-coenzyme A and undergoes complete oxidation.

Table 7 Survey of the products formed by the initial oxidative degradation reactions of the basic constituents of foodstuffs. These reactions all lead to acetyl-coenzyme A and/or the intermediates of the tricarboxylic acid cycle.

Starting material	Products of initial reactions (CO ₂ omitted)
Glucose, other hexoses	2 acetyl-coenzyme A
Fatty acids (even-numbered chains of n C-atoms)	$\frac{1}{2} n$ acetyl-coenzyme A
Fatty acids (odd-numbered chains of n C-atoms)	$\frac{1}{2} (n-3)$ acetyl-coenzyme A 1 succinate (via propionyl-coenzyme A)
Glycerol, alanine, cysteine, cystine, serine	1 acetyl-coenzyme A
Glutamic acid, histidine, arginine, ornithine, citrulline, proline, hydroxyproline	1 α -ketoglutarate
Aspartic acid	1 oxaloacetate
Leucine	3 acetyl-coenzyme A
Isoleucine	1 acetyl-coenzyme A 1 succinate (via propionyl-coenzyme A)
Valine	1 succinate (via methylmalonic semialdehyde)
Norleucine	1 acetyl-coenzyme A
Norvaline	2 acetyl-coenzyme A 1 succinate (via propionyl-coenzyme A)
α -Aminobutyric acid, homoserine, homocysteine, methionine	1 succinate (via propionyl-coenzyme A)
Glycine*	1 acetyl-coenzyme A (via serine)
Threonine	1 succinate
Lysine	2 acetyl-coenzyme A
Phenylalanine, tyrosine	1 fumarate 2 acetyl-coenzyme A
Tryptophan	at most 3 acetyl-coenzyme A**

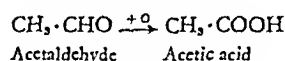
* Glycine may also be oxidized by a special cycle (see page 397).
** Other products are formed that are not oxidizable (see page 398).

In so far as substances other than carbohydrate, fat and amino acids can supply energy, their degradation follows pathways which like those of carbohydrate, fat and amino acids, yield acetyl-coenzyme A and/or an intermediate of the tricarboxylic acid cycle.

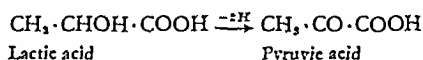
Mechanism of biological oxidations (for references see page 404)

General. The degradation reactions discussed so far take place when the foodstuff molecules are 'burned' by molecular oxygen. This 'combustion' is not, however, a direct reaction of molecular oxygen with the substrate but a transference of electrons, mediated by several complex enzyme systems, in which oxygen is the ultimate electron acceptor. In order to understand the action of the catalysts, it has to be borne in mind that biological oxidations include three types of reaction that at first sight appear to be different but are basically the same. The three types are illustrated by the following cases:

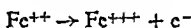
Case 1. Addition of oxygen atoms, for example:



Case 2. Removal of hydrogen atoms, for example:

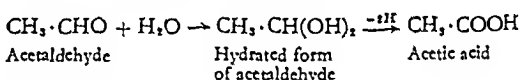


Case 3. Transformation of a metal from a lower to a higher valency state by removal of electrons, for example:

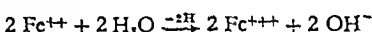


All three cases are seen to be basically similar – as removal of H atoms – if the participation of water is also considered:

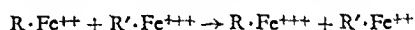
Case 1 may then be formulated as



and case 3 as



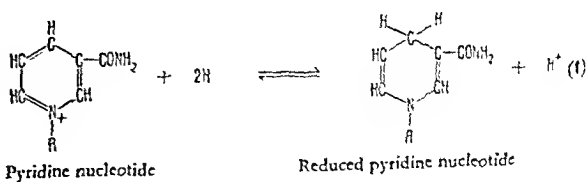
The common feature of all types of biological oxidations is a removal of electrons, although this is often either written as a removal of H (i.e., electron and proton) or as the addition of O atoms. There are instances in which neither H nor O atoms are directly involved, as in the oxidation of one heavy metal catalyst by another:

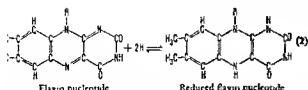


Such reactions occur in living cells between iron porphyrins (cytochromes) in which the electrons travel more or less directly from one iron atom to another. Because there are cases where electron transfer is the only change, the formulation of oxidation as electron transport is looked upon as the most general and fundamental description of this process.

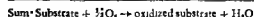
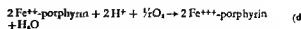
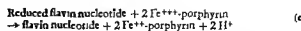
Biological oxidations may therefore be described in terms of the transfer of electrons, and the reactions whereby electrons are transferred from substrates to molecular oxygen are usually referred to as electron transport reactions.

The catalysts of biological oxidations^{1,2} Three major types of catalysts participate in biological oxidations. They are enzymes which have as prosthetic groups respectively pyridine nucleotides, flavin nucleotides and iron porphyrins. The prosthetic groups undergo reversible oxidation and reduction. The catalysts thus exist in (at least) two forms, oxidized and reduced. The mechanism of reduction is illustrated by reaction (1) for a pyridine nucleotide, and by reaction (2) for a flavin nucleotide:



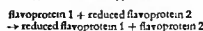


These reactions are written as similar to case 2 above. The iron atoms of iron porphyrin enzymes are reversibly oxidized and reduced as described in case 3 above.

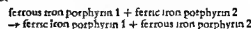


Reactions (b), (c) and (d) are referred to as the 'electron transport system' or the 'respiratory chain'.

There are many variants of this basic scheme, firstly, because there are two pyridine nucleotides, many flavoproteins (some containing nonhaem iron or molybdenum) and many iron porphyrins, secondly, because other types of reactions such as

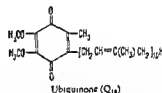
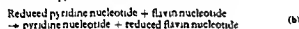
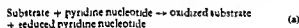


or



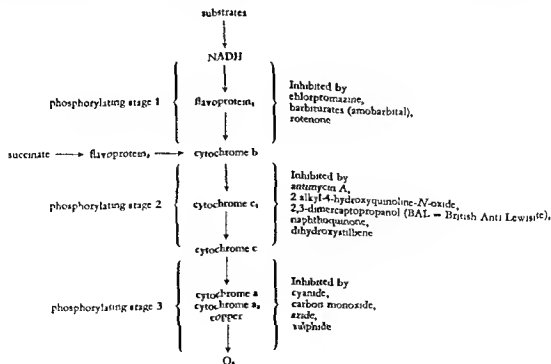
Catalyst	E_0' (volts)
Oxygen electrode ($\text{H}_2\text{O} \rightleftharpoons \frac{1}{2}\text{O}_2 + 2\text{H}^+ + 2e^-$)	+ 0.81
Cytochrome c	+ 0.25 ³
Flavin nucleotides (free)	- 0.20 ³
Pyridine nucleotides (free)	- 0.32 ³
Hydrogen electrode ($\text{H}_2 \rightleftharpoons 2\text{H}^+ + 2e^-$)	- 0.42

As seen from this table, the potentials of the electron carriers are such that the reduced form of pyridine nucleotides can act as reductant of the flavin nucleotides which, in turn, can act as reductant of the oxidized cytochromes. The order in which the catalysts transport electrons from the substrate to molecular oxygen may therefore be expressed in the following series of reactions:



Other ubiquinones differ from this structure by the number of isoprenoid units in the side chain and are accordingly called Q_1 , Q_2 , Q_3 , etc. Hydrogen transfer by these coenzymes is effected by the reversible inter-conversion of the quinone and the hydroquinone.

Fig. 8 Diagram of the pathway of electron transport showing the stages where ADP is converted to ATP and where specific inhibitors act. Electron carriers, the role of which cannot yet be clearly defined (ubiquinone, vitamin K_1 , vitamin E) have been omitted. Where the sequence in which the catalysts are arranged is uncertain they are bracketed together.



none. While the fact of reduction and reoxidation of ubiquinones is firmly established, the precise location of these catalysts in electron transport is not yet fully known. One of the places appears to be in the oxidation of succinate, another near cytochrome b₂. There is evidence that vitamin E and vitamin K are also involved in the respiratory chain².

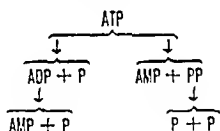
Figure 8 (page 403) illustrates schematically the pathway of electron transport and indicates the stages where ADP is converted to ATP and where specific inhibitors act.

References

- ¹ For reviews of earlier work see BALL, E.G., *Ann. N.Y. Acad. Sci.*, **45**, 363 (1944); HERBERT, D., *Ann. Rep. Progr. Chem.*, **47**, 335 (1951); SLATER, E.C., *Proceedings of the Third International Congress of Biochemistry, Brussels 1955*, New York, 1956, page 264; MAHLER and GREEN, *Science*, **120**, 7 (1954); MAHLER, H.R., *Proceedings of the Third International Congress of Biochemistry, Brussels 1955*, New York, 1956, page 252; LEHNINGER, A.L., *The Mitochondrion*, Benjamin, New York, 1964; ERNST and LEE, *Ann. Rev. Biochem.*, **33**, 729 (1964); RACKER, E., *Mechanisms in Bioenergetics*, Academic Press, New York, 1965.
- ² GRIFFITHS, D.E., in CAMPBELL and GREVILLE (Eds.), *Essays in Biochemistry*, vol. 1, Academic Press, London, 1965, page 91.
- ³ Values from BURTON, K., in KRENS and KORNBERG, *Ergebn. Physiol.*, **49**, 212 (1957).
- ⁴ WOLSTENHOLME and O'CONNOR (Eds.), *Ciba Foundation Symposium on Quinones in Electron Transport*, Churchill, London, 1961.
- ⁵ DONALDSON et al., *J. biol. Chem.*, **233**, 572 (1958); CRANE, F.L., *Biochemistry*, **1**, 510 (1962).

The key position of adenosine triphosphate (ATP) in biological energy transformations¹

One of the outstanding advances in the understanding of energy metabolism is the appreciation of the fact that the energy derived from the degradation of foodstuffs can be utilized for most purposes only if it is first transformed into a special type of chemical energy. This is the energy residing in the pyrophosphate bonds of adenosine triphosphate (ATP), which is released when these bonds are hydrolysed to form inorganic orthophosphate (P) or pyrophosphate (PP), adenosine diphosphate (ADP) and adenosine monophosphate (adenylic acid, AMP):



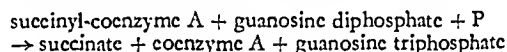
Pyrophosphate bonds release more free energy on hydrolysis (11–13 kcal according to conditions) than ester-phosphate bonds (2–4 kcal). They are therefore referred to as 'energy-rich'. It is the hydrolysis of the pyrophosphate bonds of ATP that provides the energy necessary for the various kinds of work performed by living cells, such as the contraction of muscle, the production of secretions, the activities of the nervous system and the synthesis of cell constituents.

The pyrophosphate bonds used up during the activities of the cells are resynthesized at the expense of the energy liberated by the degradation of foodstuffs. The synthesis of pyrophosphate bonds may in fact be looked upon as the first major object of the biological energy transformations. Special chemical mechanisms are required for the coupling between pyrophosphate bond synthesis and foodstuff degradation. It is evident that many hundreds of

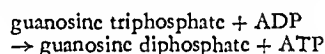
separate reactions occur when foodstuffs are degraded, but as to the special arrangement of the metabolic processes coupling degradation and pyrophosphate bond synthesis occurs at a few stages. In all, six types of reaction are known in which energy becomes available for the synthesis of ATP. Two stages occur in anaerobic glycolysis: when one molecule of glucose is converted into lactic acid two molecules of ATP are resynthesized from ADP and inorganic phosphate (Table 3, page 403). There are no more than four types of step in the course of all oxidative reactions where ATP is synthesized. The oxidative degradation of the substrate itself, i.e., the removal of two hydrogen atoms and their transfer to pyridine nucleotide, as a rule does supply energy. Energy is liberated when the hydrogen atom and electrons are transferred from the pyridine nucleotides to molecular oxygen through the reactions (b), (c) and (d) discussed on page 403. Each of these three steps leads to the synthesis of pyrophosphate bond ('oxidative phosphorylation'). The fourth of the oxidative metabolism coupled with phosphorylation consists of reactions of type (a) (page 403) where the substrate is an α -keto acid. Reactions of this type where the substrate is not an α -keto acid do not yield appreciable amounts of energy and therefore do not support the synthesis of pyrophosphate bonds.

In spite of intensive studies, the chemical mechanism by which the coupling between pyrophosphate synthesis and reactions (b), (c) and (d) is effected is still essentially unknown. For review of the present state of knowledge see the literature²⁻⁵.

Some information is available about the coupling mechanism between ATP synthesis and reactions of type (a) with α -ketonic acids as substrates. In this case an acyl-coenzyme A derivative is formed from the α -ketonic acid by the reactions described for pyruvate on page 391. Thus α -ketoglutarate yields succinyl-coenzyme A. The latter reacts as follows:



Phosphoryl succinate or phosphoryl-coenzyme A may be intermediates in this reaction though neither has as yet been identified. Guanosine triphosphate can transfer phosphate to ADP:



ATP contains two 'energy-rich' pyrophosphate bonds. It is probable that only the terminal bond serves as an immediate source of energy, or can be directly resynthesized. The second pyrophosphate bond is used to re-phosphorylate ADP according to the reaction



This reaction is catalysed by the enzyme adenylate kinase present in all tissues. The balance of this reaction plus the hydrolysis of ATP to ADP + P represents an hydrolysis of ADP to AMP + P. In reverse the reaction represents a mechanism for the re-phosphorylation of AMP.

References

- ¹ For bibliography see KREBS and KORNBERG, *Ergebn. Physiol.*, **49**, 212 (1957).
- ² SANADI et al., *Biochim. biophys. Acta (Amst.)*, **13**, 146 (1954); **14**, 434 (1954); KAUFMAN, S., *J. biol. Chem.*, **216**, 153 (1955); COHN, M., *Biochim. biophys. Acta (Amst.)*, **20**, 92 (1956).
- ³ GRIFFITHS, D.E., in CAMPBELL and GREVILLE (Eds.), *Essays in Biochemistry*, vol. 1, Academic Press, London, 1965, page 91.
- ⁴ RACKER, E., *Mechanisms in Bioenergetics*, Academic Press, New York, 1965.
- ⁵ PULLMAN and SCHATZ, *Ann. Rev. Biochem.*, **36**, 539 (1967).

Digestive enzymes

This section describes the specific enzymes the combined action of which is responsible for the digestion of foodstuffs. Each enzyme catalyses the hydrolysis of one compound or of a series of closely related compounds. (For a general review of enzymes and enzyme action see pages 382-386)

Catalytic enzymes (proteases, peptide hydrolases, peptidases)

These are enzymes catalysing the hydrolytic cleavage of peptide bonds



They may be divided into two main classes

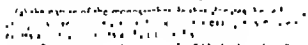
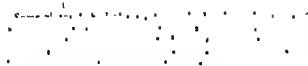
1 *Peptidyl-peptide hydrolases (endopeptidases)*, which act on proteins and peptides by hydrolysing 'internal' peptide linkages, i.e. those situated away from the ends of peptide chains.

2 *α -Amino-acyl-peptide hydrolases, peptidyl-amino-acyl hydrolases (exopeptidases)*, which catalyse the hydrolysis of peptide bonds situated at the ends of peptide chains. These enzymes are specific for peptides possessing one or more free terminal α -amino or α -carboxyl groups

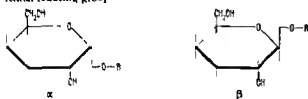
Members of both classes of proteases are widely distributed in mammalian tissues. Those of the gastrointestinal tract are discussed in Tables 10 and 11, pages 406-409, those of other tissues in Table 12 (pages 410-411)

Glycoside hydrolases (glycosidases)

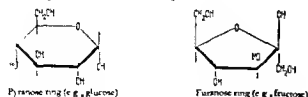
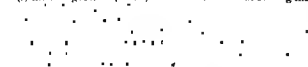
Carbohydrates are digested by these enzymes, which catalyse the hydrolysis of glycosidic bonds



tential reducing group



(i) the configuration (D or L) of the monosaccharide bearing the



Pyranose ring (e.g., glucose)

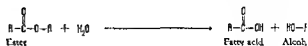
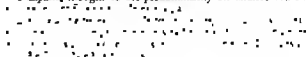
Furanose ring (e.g., fructose)

The general properties of mammalian glycoside hydrolases are described in Table 13 (pages 411-413). For their content in the mucus of the human small intestine see page 413

Lipases and other ester hydrolases (esterases)

Fats and other esters are hydrolysed by the action of enzymes that have been subdivided into

1 *Lipases*, thought to act predominantly on undissolved oil



have similarly, like those of the gastrointestinal tract, they hydrolyse fats and short-chain fatty acid esters

Phosphoric ester hydrolases (phosphatases)

Mammalian tissues contain a variety of unspecific esterases which have not yet been obtained in a pure form. Some of these enzymes

classified as

1 *Phosphoric monoester hydrolases (phosphomonoesterases)*, hydrolysing monoesters of phosphoric acid



For example, glucose 6-phosphate is hydrolysed to glucose and phosphate

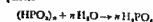
2 *Phosphoric diester hydrolases (phosphodiesterases)*, hydrolysing substrates such as nucleic acids, or the synthetic substrate diphenyl or triphenyl phosphate, at one of the ester linkages



3 *Pyrophosphatases*, hydrolysing the pyrophosphate linkages of salts of pyrophosphoric acid and of pyrophosphate esters



4 *Metaphosphatases*, hydrating metaphosphates to orthophosphates

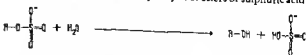


These have not been demonstrated to occur in the mammalian body

The phosphoric ester hydrolases are described in Table 15 (page 415-416), those acting on phospholipids and their metabolic products in Table 16 (page 417)

Sulphuric ester hydrolases (sulphatases)

These enzymes catalyse the hydrolysis of esters of sulphuric acid



They may be distinguished according to the nature of the sulphuric acid esters they hydrolyse

Nucleases

Ribonucleases (RNAases) and deoxyribonucleases (DNAases) catalyse the cleavage of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) respectively (Table 17, pages 418-419). They are present in most if not all tissues.

Of the RNAases only pancreatic RNAase has been studied extensively. The enzyme is a specific phosphodiesterase hydrolysing certain phosphoric ester linkages of RNA but not of DNA. The end-products of the prolonged action of pancreatic RNAase are 3'-uridylic acid, 3'-cytidylic acid, and a large number of dialysable polynucleotides of varying degrees of polymerization. The terminal nucleotides of these polynucleotides are all either 3'-uridylic acid or 3'-cytidylic acid.

The initial action of RNAase on RNA probably involves mainly the 'phosphotransferase' action of the enzyme. The first step consists of the cleavage of the phosphodiester bond between the 3'- and 5'-positions of the ribose moieties of the RNA molecule, with the formation of oligonucleotides terminated by cyclic 2',3'-phosphates. These terminal groups are split off (when the preceding unit in the RNA chain contains pyrimidine) as free mononucleotide

Fig. 9 Reactions catalysed by pancreatic ribonuclease

The 5'-ester linkages attacked are indicated by broken arrows, those not attacked by crossed arrows. The enzyme does not attack 3'-ester linkages.

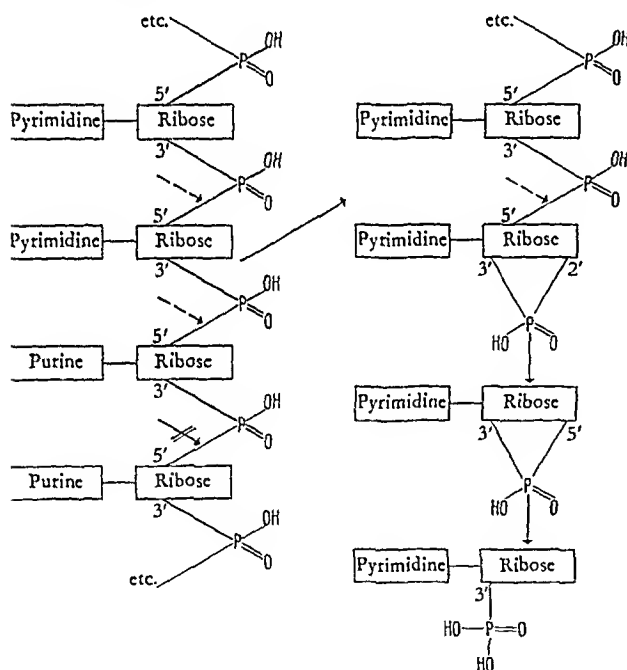
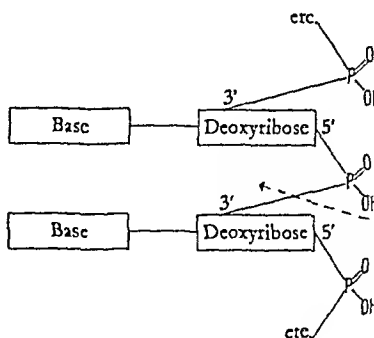


Fig. 10 The specificity of pancreatic deoxyribonuclease

The ester linkage attacked by the enzyme is indicated by a broken arrow.



cyclic phosphates and are then hydrolysed with the formation of the corresponding nucleoside 3'-phosphate². The mode of attack of the enzyme on a hypothetical part of an RNA molecule is shown in Figure 9. Several enzymes have been reported to attack RNA with the production of nucleoside 5'-phosphates.

Several types of DNAases are present in various tissues³; of these, pancreatic DNAase (DNAase I) has been studied most extensively. The enzyme is a specific phosphodiesterase that hydrolyses certain phosphoric ester linkages of DNA. Some preparations appear to act also on RNA. The end-products of the prolonged action of DNAase on DNA are mainly di- and tri-nucleotides as well as small amounts of mononucleotides and other polynucleotides. A the fragments produced are 5'-nucleotides. This indicates that pancreatic DNAase specifically hydrolyses nucleoside 5'-phosphodiester with the resulting liberation of the corresponding nucleoside 5'-phosphates (Figure 10). The enzyme appears to have a preference for action on linkages between purine and pyrimidine nucleotides. A DNAase from spleen and thymus (DNAase II) differs from DNAase I in many of its properties. In particular DNA digestion by DNAase II produces more mononucleotides, considerably fewer dinucleotides, and much larger amounts of the higher oligonucleotides. All these reaction products are terminated by 3'-phosphates.

The products of the action of RNAase and DNAase are broken down further by other phosphodiesterases and phosphatases (see Table 17, pages 418-419) to yield nucleotides and nucleosides. The latter are then degraded by phosphorolysis to yield purines and pyrimidines and pentose 1-phosphate, or by hydrolysis to yield purines and pyrimidines, pentose and inorganic phosphate.

References

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Table 10 Peptidyl-peptide hydrolases (proteases) and their precursors in the gastrointestinal tract (for references see page 408)

Enzyme	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalysed*	Remarks
Pepsinogen (enzyme precursor)	Chief cells of gastric mucosa	43 000	-	-	Formation of pepsin from pepsinogen is autocatalytic at pH < 5 (maximally at pH 2) with loss of (a) 'pepsin inhibitor', containing 29 amino acids, of mol. wt. 3242, and (b) 5 smaller peptides of aggregate mol. wt. ca. 4000. ^{2,3}

* The specificity relationships listed are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of the enzymes acting on proteins *in vivo*.

16 10 (continued) Peptidyl-peptide hydrolases (proteases) and their precursors in the gastrointestinal tract

Enzyme*	Location	Approx. mol wt	Optimal pH of action	Reaction catalysed**	Remarks
1.4.1.1 Pepsin	Gastric juice	36 000	1.8-4.4 Depends on the nature of the substrate*	$\begin{array}{c} R & R \\ & \\ -CO-NH-CH-CO- & -NH-CH-CO- \end{array}$	Endopeptidase attacks most 1 tens except some prolamines keratins Denatured proteins cham
1.4.2.1 Pepsin B*	Gastric juice	36 000	ca 3	Similar to pepsin	Formerly known as parapep Differs from pepsin in the terminal amino-acid residue, p phorus content, and stability pH 6.9*
1.4.2.2 Gastricsin*	Gastric juice	-	ca 3	Similar to pepsin	More heat-stable than pepsin has a lower electrophoretic m ity on starch gel; could be autolysis product of pepsin*
3.4.4.3 Rennin	Stomach of young animals	40 000	Milk clotting ca. 5, proteolysis (haemoglobin) 3.7*	Similar to pepsin* The crys- talline enzyme (unlike com- mercial rennet) does not have phosphoramidase activity	Clots milk and liberates pep from the α -casein cont therein
Trypsinogen (enzyme precursor)	Pancreas	24 500 ¹²	-	-	Nonenzymatic precursor of t sin, into which it is converted enteropeptidase and, autocata cally, by trypsin, with elimin of a hexapeptide of structure (Asp)-Lys from the N-term end by scission of a Lys-Ile b
3.4.4.4 Trypsin	Intestinal secretion	23 800	7-8	-	-
Chymotrypsinogen A (enzyme precursor)	Acinar cells of pancreas	25 000 ¹²	-	-	-
Chymotrypsinogen B ¹³ (enzyme precursor)	Acinar cells of pancreas	21 600 ¹⁴	-	-	-

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386).

** The specificity relationships listed are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of enzymes acting on proteins *in vivo*.

Table 10 (concluded) Peptidyl-peptide hydrolases (proteases) and their precursors in the gastrointestinal tract

Enzyme*	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalysed**	Remarks
3.4.4.5 <i>Chymotrypsin A</i>	Pancreas	25 000	7.8	$\begin{array}{c} R \quad \quad R' \\ \quad \quad \\ -CO-CH-NH- \quad -CO-CH-NH- \\ \\ \text{where for maximum activity} \\ R' \text{ is phenyl or substituted phenyl. However, other bonds} \\ \text{(such as L-leucyl or L-asparaginyl)}^{1,4} \text{ are also split at high rates} \end{array}$	Derived from chymotrypsinogen A; contains three open peptic chains held together by disulphic bridges. Unlike trypsin, clots milk but not blood. Irreversibly inhibited by <i>p</i> -nitrophenyl phosphate ¹
3.4.4.6 <i>Chymotrypsin B</i>	Pancreas	23 600 ¹⁶	ca. 8	Similar to chymotrypsin A	Unlike chymotrypsin A, splits acyl tryptophan esters very slowly in presence of 30% methanol ¹⁸
3.4.4.7 <i>Pancreaticopeptidase E</i> ¹⁹	Pancreas	—	ca. 8	Hydrolyses peptide linkages, preferentially those adjacent to neutral L-amino-acid residues	Formerly known as elastase
3.4.4.8 <i>Enteropeptidase</i>	Intestinal secretion	—	ca. 6	Converts trypsinogen to trypsin	Exact mode of action unknown, since maximal activation of trypsinogen occurs under conditions where autocatalytic activation is also maximal. Enteropeptidase is probably a glycoprotein ²⁰

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386).

** The specificity relationships listed are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of the enzymes acting on proteins *in vivo*.

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Table 11 α -Aminoacyl-peptide hydrolases and peptidyl-amino-acid hydrolases in the gastrointestinal tract¹

A large number of different exopeptidases have been recognized as occurring in the gastrointestinal tract. They are distinguished from each other mainly in their specificity of action on synthetic peptides. Relatively few have been purified extensively, and the list given here includes only those that have been well characterized.

Enzyme*	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalysed**	Remarks
<i>Dipeptidases:</i> 3.4.3.1 <i>Glycyl-glycine dipeptidase</i> 3.4.3.6 <i>Iminodipeptidase</i> (prolinase) 3.4.3.7 <i>Imidodipeptidase</i> (prolidase)	Intestinal secretions	—	ca. 8	Hydrolyse dipeptides, with various degrees of specificity	The component members of this class of enzymes have not yet been sufficiently characterized to merit individual description. Glycyl-glycine dipeptidase ² appears to be highly specific for this peptide linkage. Iminodipeptidase appears to act only on dipeptides which bear the free imino group of L-proline or hydroxy-L-proline ² , whereas imidodipeptidase splits peptide bonds involving the nitrogen of these compounds ²

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386).

** The specificity relationships listed are those elucidated by the action of the enzymes on synthetic peptides; they are not necessarily those of the enzymes acting on proteins *in vivo*.

Table 11 (continued) α -Aminoacyl-peptide hydrolases and peptidyl-amino-acid hydrolases in the gastrointestinal tract

Enzyme*	Location	Approx. mol. wt.	Optimal pH of action	Reaction catalysed**	Remarks
Procarboxypeptidase A (enzyme precursor)	Acinar cells of pancreas	96000	-	-	Nonenzymatic precursor of carboxypeptidase A. Is more acidic and larger than the enzyme to which it is converted by trypsin. In this process, approx. 40 small peptides (average mol. wt. ca. 1500) are released, but the enzymatic activity is confined to carboxypeptidase A.
3421 Carboxypeptidase A	Pancreatic juice	34000	7.5-8.5	$\begin{array}{c} R \\ \\ RCO-NH-CH(COOH) \end{array}$ <p>Hydrolyses terminal peptide linkage adjacent to free carboxyl group. Though of wide specificity, maximally active when R' = aromatic nucleus</p>	Contains Zn (ca. 1.9 mg/g) as essential constituent
3422 Carboxypeptidase B	Pancreatic juice	-	ca. 8	$\begin{array}{c} R \\ \\ RCO-NH-CH(COOH) \end{array}$ <p>Acts uniquely on peptides containing R' = arginine, lysine or ornithine. Again, carboxyl group must be free*</p>	Formed from procarboxypeptidase B by tryptic activation*. Probably identical with 'protrypsin'*
3411 Leucine aminopeptidase	Small intestine	300000*	ca. 8	$\begin{array}{c} R \\ \\ R_1CH(COOH)-CH(R_2)-NH-CH(COOH) \end{array}$ <p>Wide specificity? Active when R = Leu. Also attacks p- but more slowly</p>	Also found in other tissues, plants and micro-organisms. Activated by Mg^{++} or Mn^{++} , inhibited by anions Cl^{-} , SO_4^{--} , CO_3^{--}
3413 Aminopeptidase*	Small intestine	-	7.5-8.5	$\begin{array}{c} R \\ \\ R_1CH(COOH)-CH(R_2)-CH(R_3)-NH-CH(COOH) \end{array}$ <p>Hydrolyses a wide range of tripeptides. R = amino group</p>	Hydrolyses tripeptides at the bond adjacent to the carboxyl group

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386)

** The specificity relationships listed are those elucidated by the action of the enzymes on synthetic peptides, they are not necessarily those of the enzymes acting on proteins *in vivo*

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Table 12 Peptidyl-peptide hydrolases and exopeptidases in tissues other than the gastrointestinal tract

Enzyme*	Location	Optimal pH of action	Reaction catalysed**	Remarks
<i>Peptidyl-peptide hydrolases</i>				
– <i>Cathepsins*** A and B</i> ¹	Ubiquitous component of animal tissues; particularly abundant in spleen, liver, kidney and lung	ca. 4 (A); 5–6 (B)	Similar in action to pepsin (A) and trypsin (B): can effect the activation of trypsinogen ²	Whereas A requires no activator, B has an absolute requirement for –SH compounds
3.4.4.9 <i>Cathepsin C</i>	Ubiquitous but most abundant in spleen	ca. 5 (at higher pH, catalyses transamidation reactions ³)	Similar in action to chymotrypsin but more restricted in its specificity: attacks only peptide linkages at a specified distance from the free α -amino group ³	Activated by –SH compounds by cyanide
3.4.4.23 <i>Cathepsin D</i> ⁴	Spleen	3.0 (acid-denatured haemoglobin); 4.2 (acid-denatured albumin)	Similar in action to pepsin, but more restricted in specificity	Does not hydrolyse the synthetic substrates ³ hydrolysed by cathepsins A, B and C. The enzyme is heat-labile and rapidly destroyed below pH 2.5
3.4.4.13 <i>Thrombin</i>	Blood serum	ca. 7	Hydrolyses peptides, amides and esters of L-arginine; converts fibrinogen to fibrin	Formed from the nonenzymic precursor prothrombin by a variety of factors ⁵
3.4.4.14 <i>Plasmin</i>	Blood serum	ca. 7	Hydrolyses peptides and esters of L-arginine and L-lysine; converts fibrin into soluble products	Formed from plasminogen ⁶
<i>Exopeptidases</i>				
3.4.3.1 <i>Glycyl-glycine dipeptidase</i>	Many tissues; has been partially purified from rat muscle, human uterus and swine kidney ⁷	7.6	Similar in action to the intestinal enzyme	Activity enhanced by addition of Co ⁺⁺ or, more weakly, of Mn ⁺⁺ . Preparations of this enzyme from rat muscle are exceedingly unstable, from human uterus less so
3.4.3.2 <i>Glycyl-leucine dipeptidase</i>	Several tissues; has been partially purified from uterus ⁷	ca. 8	Similar in action to the intestinal enzyme	Activity enhanced by Zn ⁺⁺ and phosphate
3.4.3.3 <i>Carnosinase</i>	Several tissues; has been partially purified from spleen, liver and swine kidney ^{7,8}	8.0–8.4 in presence of Mn ⁺⁺ ; 7.8–7.9 in presence of Zn ⁺⁺ ; 7.4–7.5 in absence of metal	A dipeptidase, hydrolysing L-alanyl-L-histidine > glycyl-L-histidine > β -alanyl-L-histidine > D-alanyl-L-histidine	Activity enhanced by Zn ⁺⁺ and Mn ⁺⁺
3.4.3.6 <i>Iminodipeptidase (prolinase)</i>	Many tissues; has been partially purified from swine kidney ⁷	ca. 8	Similar in action to the intestinal enzyme	Activity enhanced by Mn ⁺⁺ and Cd ⁺⁺
3.4.3.7 <i>Imidodipeptidase (prolidase)</i>	Many tissues; has been found in skeletal and smooth muscle, erythrocytes, serum, pituitary, lung and kidney, and has been partially purified from equine erythrocytes and swine kidney ⁷	7.8–8.0	Similar in action to the intestinal enzyme	Activity enhanced by Mn ⁺⁺
3.4.2.1 <i>Carboxypeptidase A</i>	Most animal tissues	ca. 7	Homospecific with pancreatic carboxypeptidase A	Old name: cathepsin IV

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386).

** The specificity relationships listed have been elucidated by the use of synthetic substrates; they are not necessarily those of the enzymes acting on proteins *in vivo*.

*** The term 'cathepsin' is applied to proteinases obtained from tissues other than the gastrointestinal tract. None of them has yet been crystallized and their physiological role is not established.

Table 12 (continued) Peptidyl-peptide hydrolases and exopeptidases in tissues other than the gastrointestinal tract

Enzyme*	Location	Optimal pH of action	Reaction catalysed**	Remarks
<i>Exopeptidases (continued)</i>				
3.4.1.1 <i>Leucine aminopeptidase</i>	Many tissues; especially abundant in kidney	8-9		
3.4.1.3 <i>Aminopeptidase</i>	Most animal tissues	8.0	Similar in action to intestinal tripeptidase	Inhibited by cysteine, Cd^{++} , Hg^{++} . Rapidly inactivated in acid media

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386)

** The specificity relationships listed have been elucidated by the use of synthetic substrates; they are not necessarily those of the enzymes acting on proteins *in vivo*

References

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Table 13 Glycosyltransferases and glycoside hydrolases (glycosidases) (for references see page 413)

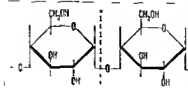
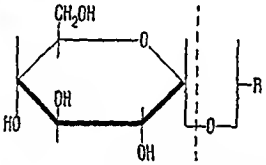
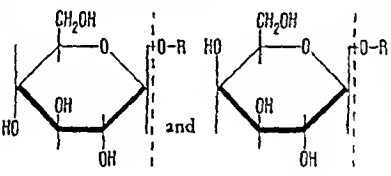
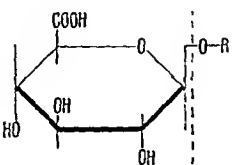
Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
2.4.1.1 α -Glucan phosphorylase [†] (glycogen phosphorylase)	Muscle, liver	6.9	Transfers D-glucose residues from non-reducing end of starch or glycogen chains to inorganic phosphate, D-glucose or oligosaccharides α -D-glucose 1-phosphate + $[\text{G}]_n \rightleftharpoons [\text{G}]_{n+1} + \text{H}_2\text{PO}_4$	Acts on glycogen and amylopectin. Phosphorolysis of exterior chains giving 20-44% α -D-glucose 1-phosphate from various glycogens and 35-55% from various amylopectins and leaving a phosphorylase limit dextrin (Φ -dextrin). Most phosphorylases exist in more than one form, an <i>a</i> form active in the absence of adenosine 5' phosphate and a <i>b</i> form dependent on adenosine 5'-phosphate for activity. Pyridoxal 5'-phosphate is a prosthetic group for <i>a</i> and <i>b</i> forms. Interconversion of <i>a</i> and <i>b</i> forms is an enzymic process involving the action of a specific phosphatase (<i>a</i> \rightarrow <i>b</i>) or a phosphokinase (<i>b</i> \rightarrow <i>a</i>). This change is accompanied by a gross change in molecular size.
3.2.1.1 α -Amylase [†]	Saliva, pancreatic juice, blood	6.9		Hydrolyses in a random manner non-terminal α -1,4-glucosidic bonds in amylose, amylopectin, glycogen and dextrin. The initial step of the reaction is the formation of a covalent intermediate between the enzyme and the substrate. Products of the enzyme reaction are maltose (70-90%), small amounts of D-glucose, and α limit dextrins consisting of 4-8 glucose units and containing one or more α -1,6-glucosidic linkages [†] . The α -amylases are calcium metalloproteins whose activity is enhanced by $\text{Cl}^- > \text{Br}^- > \text{I}^- > \text{NO}_3^-$.

Table 13 (continued) Glycosyltransferases and glycoside hydrolases (glycosidases)

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
3.2.1.10 <i>Oligo-1,6-glucosidase</i> ³	Small intestine	6.3	Hydrolyses 1,6-glucoside linkages of isomaltose, panose, and α -amylase dextrins	Participates in the digestion of starch by hydrolysing the α -amylase limit-dextrins to smaller unbranched molecules that can be further degraded by α -amylase and α -glucosidase in the pancreatic juice. Has no action on glycogen, phosphorylase limit-dextrin or maltose
3.2.1.33 <i>Dextrin-1,6-glucosidase</i> ⁴ (a similar enzyme from plants is listed 3.2.1.9)	Muscle	ca. 7	Hydrolyses the outermost inter-chain linkages in a phosphorylase limit-dextrin to give glucose + polysaccharide	Originally known as amylo-1,6-glucosidase. Hydrolyses the α -1,6-glucosidic bonds of the limit-dextrin resulting from phosphorylase action. The enzyme liberates glucose plus a polysaccharide that can again be degraded by phosphorylase action. The concurrent action of dextrin-1,6-glucosidase and phosphorylase gives complete breakdown of the polysaccharide yielding >90% α -D-glucose 1-phosphate and D-glucose (4-8%) from the α -1,6-linked residues. This enzyme differs from oligo-1,6-glucosidase in having no action on isomaltose, panose, or α -amylase limit-dextrin. In the relative absence of this enzyme, as in type 3 glycogen-storage disease (see pages 450 to 451), glycogen breakdown is incomplete and limited to the exterior chains
3.2.1.20 <i>α-Glucosidase</i>	Small intestine, pancreatic juice, blood, liver	6.6-7.0	 where R = glucose (in which case the compound is maltose), substituted hexoses, phenols, terpenes, etc.	Formerly called maltase: the maltose produced from the digestion of starch by α -amylase is hydrolysed to glucose by this enzyme. Inhibited by the glucose formed. Certain α -glucosidases hydrolyse sucrose and others do not. At least three intestinal 'maltases' have been separated from 'isomaltase' ^{3, 6}
3.2.1.21 <i>β-Glucosidase</i> 3.2.1.23 <i>β-Galactosidase</i> ⁵	Kidney, liver, small intestine, blood	ca. 6	 and	β -Glucosidase is widespread in plants and micro-organisms. In some preparations it appears to be identical with β -galactosidase ⁷ . β -Galactosidases can transfer galactose residues to a variety of acceptors (such as lactose, galactose and glucose) as well as to water
3.2.1.31 <i>β-Glucuronidase</i> ⁸	All mammalian tissues and body fluids; especially high in liver, kidney, spleen, epididymis and cancer tissues	ca. 5	 Hydrolyses steroid glucuronides and various β -glucuronides excreted in urine and bile	Possibly plays a role in mucopolysaccharide metabolism. Hydrolyses alkyl, aryl, alicyclic and acyl β -glucuronides and some β -galacturonides. Aldonolactones are powerful competitive inhibitors of the enzyme. Dilute solutions of the enzyme are activated non-specifically by a variety of high molecular weight compounds, the most reliable results being given by albumin. No action on α -glucuronides or β -glucosides. Shows some transference reaction <i>in vitro</i> but unlikely to be of importance in glucuronide synthesis <i>in vivo</i> . After the action of testicular hyaluronidase on hyaluronic acid or chondroitin, the oligosaccharides formed are degraded stepwise from the non-reducing end by β -glucuronidase and β -acetylglucosaminase (below) acting alternately

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385-386).

13 (continued) Glycosyltransferases and glycoside hydrolases (glycosidases)

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
1.1.35 <i>α</i> -uronate lyase hyaluronidase ⁹	Testes	ca. 7		products of action on chondroitin sulphates are tetrasaccharides, apparently still 4- and 6-sulphate esters. The hyaluronidase contained in the head of most mammalian spermatozoa probably plays a role in their penetration through the granulosa cell layer of the ovum
2.1.17 <i>Isocopeptidase</i> glucosylase ¹⁰ (lysozyme)	Tears, nasal mucus, saliva, blood serum and plasma	6.2		a role in defending mucus surfaces against bacterial invasion
3.2.1.19 <i>Heparinase</i> ¹¹	Liver and kidney	5.3-6.8	Hydrolyses α-1,4 links between D-glucosamine sulphate and D-glucuronic acid residues in heparin	A similar enzyme isolated from bacteria has been used to elucidate the structure of heparin ¹²
3.2.1.30 D-Acetylglucosaminase ¹³	Spleen, liver, kidney, lung, blood, heart, brain, testes	4.0-6.0		glucose residues from A but not from O(H) ¹⁴ . The same enzyme may act on β-acetylglactosaminases

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386).

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¹⁴ J. H. HAN, *Biochem. J.*, 76, 257 (1960)

Glycoside hydrolases of the mucus of the human small intestine¹

Age	Number	Protein (mg/g mucus)	Enzyme activity (U/g protein)*				
			*Maltase	*Saccharase	*Isomaltase	*Lactase	*Amylase ²
Gestational age							
2-3 months	2	42.5	12.5 (2.1-23)	4 (0.6-7.5)	4 (0.6-7.4)	1	
3-4 months	3	51 (47-55)	104 (80-124)	40 (34-48)	36 (36-37)	7 (5-9)	
6 months	1	90	132	52	44	15	5
7-8 months	6	96 (58-150)	235 (100-451)	91 (31-201)	74 (35-145)	26 (15-37)	6.6
8-9 months	10	90 (77-127)	281 (138-422)	101 (51-150)	85 (37-113)	31 (16-77)	11.4 (8-18)
Adults	15	90 (84-121)	246 (70-456)	76 (24-152)	74 (27-132)	33 (5.9-54.5)	16.9 (8.8-32)
						6.8 (1-11.1)	205 (78-117)

* 1U = 1 μmol disaccharide hydrolysed per minute at 37°C and pH 5.5

² AGRICCHIO et al., *Pediatrics*, 35, 944 (1965)

Table 14 Fatty acid ester hydrolases (fatty acid esterases)

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
3.1.1.1 <i>Carboxylesterase</i> ¹	Most tissues, high activity in liver	ca. 8	Hydrolyses carboxylic esters to give a carboxylic acid and an alcohol	Formerly called aliesterase. Hydrolyses dissolved triglycerides. Much more active on simple esters (e.g., methyl butyrate) than on acetylcholine. All esterases can catalyse the transfer of the acyl moiety of the substrate. In the presence of hydroxylamine the liver enzyme catalyses the formation of hydroxamic acids from fatty acids ²
3.1.1.3 <i>Lipase</i> ³	Pancreas, gastric juice, saliva	7-9	$\begin{array}{c} \text{CH}_2-\text{O}-\text{CO}-\text{R} \\ \\ \text{CH}-\text{O}-\text{CO}-\text{R}' \\ \\ \text{CH}_2-\text{O}-\text{CO}-\text{R}'' \end{array}$ where R, R' and R'' are long-chain fatty acids. Attacks tri- > di- > monoglycerides	Splits preferentially the outer chains of the triglyceride so that hydrolysis proceeds via triglyceride → 1,2-diglyceride → 2-mono-glyceride → glycerol. Pancreatic lipase acts only at an ester-water interface. Suspensions of methyl butyrate and triacetin are readily hydrolysed but the enzyme does not attack true solutions of methyl butyrate. Bile salts activate the enzyme, in part by emulsifying the water-insoluble substrate. The optimum reaction for hydrolysis of lower triglycerides is about pH 7. For higher triglycerides it is pH 8.8
3.1.1.6 <i>Acetylesterase</i> ¹	Widely distributed	ca. 7	Hydrolyses acetic esters to give an alcohol and acetic acid	Also attacks aromatic acetates. Less sensitive to eserine inhibition than cholinesterase
3.1.1.7 <i>Acetylcholinesterase</i> ⁴	Most tissues, especially conductive tissues (e.g., brain, nerves), erythrocytes	ca. 7	Hydrolyses acetylcholine to give acetic acid and choline. Hydrolyses propionylcholine at the same rate but butyrylcholine only slowly	Has a well-defined optimum substrate concentration for acetylcholine of 4-7 μmol/ml and is inhibited at higher concentrations. Acetyl-β-methylcholine is rapidly hydrolysed, but the rate is considerably lower than with acetylcholine. Acts on a variety of acetic esters and catalyses transacetylations
3.1.1.8 <i>Cholinesterase</i> ⁵	Most tissues, especially blood serum, pancreas, liver, ovary, placenta, intestinal mucosa, brain	ca. 7	Hydrolyses acylcholine to give choline and an acid	Hydrolyses butyryl- or propionylcholine more rapidly than acetylcholine. Also hydrolyses simple butyryl or propionyl esters. Does not act on acetyl-β-methylcholine. Does not have a well-defined substrate optimum, i.e., is not inhibited by excess substrate. The cholinesterases can be distinguished from the simple esterases by the effect of eserine (physostigmine). All types of cholinesterase are completely inhibited by 10 ⁻³ -molar eserine
3.1.1.13 <i>Cholesterol esterase</i> ⁶	Pancreas, blood serum	ca. 8	Hydrolyses cholesterol esters to give cholesterol and an acid	The enzyme from pancreas has an absolute requirement for free cholic acid. The enzyme is much less stable than lipase. Purified enzyme has synthetic as well as hydrolytic activity. Cholesterol, dehydroandrosterone, dihydrocholesterol and cholestanol are readily esterified and all the steroid butyrates are rapidly hydrolysed. Cholesterol esterase may be identical with one of the carboxylesterases of the pancreas

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386).

References

¹ HOFSTEE, B.H.J., in BOYER et al. (Eds.), *The Enzymes*, 2nd ed., vol. 4, Academic Press, New York, 1960, page 485.

² LIPMANN and TUTTLE, *Biochim. biophys. Acta* (Amst.), 4, 301 (1950).

³ DESNUELLE, P., *Advan. Enzymol.*, 23, 129 (1961).

⁴ WILSON, I.B., in BOYER et al. (Eds.), *The Enzymes*, 2nd ed., vol. 4, Academic Press, New York, 1960, page 501.

⁵ AUGUSTINSON, K.-B., in BOYER et al. (Eds.), *The Enzymes*, 2nd ed., vol. 4, Academic Press, New York, 1960, page 521.

⁶ HERNANDEZ and CHAIKOFF, *J. Biol. Chem.*, 228, 447 (1957).

No 15 Phosphatases

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
3.1.3 Phosphoric acid monoester hydrolases (phosphomonoesterases)				
1.3.1 <i>Alkaline phosphatase¹</i>	Most cells, particularly zones of growth of bones, intestinal mucosa, kidney, lactating mammary gland, milk	9-10, depending on substrate and concentration	$ \begin{array}{c} \text{OH} \\ \\ \text{O} - \text{P} - \text{O} - \text{R} \\ \\ \text{OH} \\ \\ \text{HO} + \text{H} \end{array} $	Has wide specificity. Activity is enhanced by divalent cations, e.g., Mg^{++} . In contrast to certain other groups of hydrolases, phosphomonoesterhydrolases and phosphodiesterases are not inhibited by di-isopropyl fluorophosphate. The enzyme shows transferase activity. In hypophosphatasia abnormally low amounts of the enzyme are present in all tissues and in blood serum. In bone destruction the amount in blood serum is considerably increased. Might serve to provide inorganic phosphate for metabolic, excretory and some secretory purposes.
3.1.3.2 <i>Acid phosphatase²</i>	Lactating mammary gland, kidney, prostate, liver, spleen, erythrocytes	5.3-5.6	As for alkaline phosphatase	Has wide specificity. Many but not all acid phosphatases catalyse transfer of the phosphoryl group to organic hydroxyl compounds. Of the animal acid phosphatases only the enzyme from prostate glands is inhibited by (+) tartrate.
3.1.3.9 <i>Glucose-6-phosphatase³</i>	Liver, kidney, small intestine	6.5	$ \begin{array}{ccc} \begin{array}{c} \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{CH}_2\text{OPO}_3\text{H}_2 \\ \\ \text{H}_2\text{N} \\ \text{Glucose 6-phosphate} \end{array} & \longrightarrow & \begin{array}{c} \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{CH}_2\text{OH} \\ \text{Glucose} \end{array} + \text{H}_3\text{PO}_4 \end{array} $	Readily catalyses the transfer of a phosphoryl group from glucose 6-phosphate to glucose or fructose. Hydrolytic activity is inhibited by glucose. Appears to be solely associated with the microsomal fraction. Plays a role in the formation of glucose from glycogen and noncarbohydrate compounds (see Fig 17, page 441). Absent from, or weak in, the liver during glycogen storage disease ⁴ .
3.1.3.11 <i>Fructose-6-phosphatase</i>	Kidney, liver	9.3-9.5	$ \begin{array}{ccc} \begin{array}{c} \text{H}-\text{OH} \\ \\ \text{CH}_2\text{O}-\text{PO}_3\text{H}_2 \\ \\ \text{C}=\text{O} \\ \\ \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{CH}_2\text{OPO}_3\text{H}_2 \\ \text{Fructose 1,6-diphosphate} \end{array} & \longrightarrow & \begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{C}=\text{O} \\ \\ \text{HO}-\text{C} \\ \\ \text{HO}-\text{C} \\ \\ \text{CH}_2\text{OPO}_3\text{H}_2 \\ \text{Fructose 6-phosphate} \end{array} + \text{H}_3\text{PO}_4 \end{array} $	Markedly specific for fructose 1,6-diphosphate ⁵ . Does not hydrolyse glucose 1-phosphate, glucose 6-phosphate, fructose 6-phosphate, L-sorbose 1-phosphate or phosphoglycerate. Fructose 1-phosphate and L-sorbose 1,6-diphosphate are hydrolysed at rates of 0.009 and 0.03 times the rate for fructose 1,6-diphosphate respectively. The enzyme is activated by Mg^{++} or Mn^{++} and inhibited by fructose 6-phosphate, fructose 1,6-diphosphate and adenosine monophosphate. Plays a role in the synthesis of glycogen from noncarbohydrate compounds (see Fig 17, page 441).

Table 15 (continued) Phosphatases

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
3.1.4 Phosphoric acid diester hydrolases (phosphodiesterases)				
3.1.4 <i>Phosphodiesterases</i>	Widespread	—	Hydrolyses phosphoric diesters to a phosphoric monoester and an alcohol	The enzymes classified as phosphodiesterases are listed elsewhere, e.g., glycerophosphorylcholine diesterase, phospholipase C and phospholipase D in Table 16 opposite, and ribonuclease, deoxyribonuclease and phosphodiesterase in Table 17, page 441
3.6.1 Hydrolases acting on anhydrides containing phosphoryl				
3.6.1.1 <i>Inorganic pyrophosphatase</i> ⁶	Liver, brain, erythrocytes and other tissues	7.6–7.8	$\begin{array}{c} \text{OH} \quad \text{OH} \\ \quad \\ \text{O}=\text{P}-\text{O}-\text{P}=\text{O} \\ \quad \\ \text{OH} \quad \text{OH} \\ \\ \text{HOH} \end{array} \longrightarrow 2 \text{H}_3\text{PO}_4$	Has an absolute requirement for Mg ⁺⁺ . Some tissues contain a pyrophosphatase with an acid pH optimum, and this enzyme is not stimulated by Mg ⁺⁺
3.6.1.7 <i>Acylphosphatase</i> ⁷	Skeletal muscle, brain, kidney, liver, leucocytes	5.3	$\begin{array}{c} \text{OH} \\ \\ \text{O}=\text{P}-\text{O}-\text{CO}-\text{R} \\ \\ \text{OH} \\ \\ \text{HOH} \end{array}$ <p>where R·CO = acetyl, butyryl, palmityl</p>	Also catalyses the hydrolysis of 1,3-diphosphoglyceric acid and carbamyl phosphate. No reaction with glycerol phosphate, 3-phosphoglycerate or phosphoenolpyruvate. Stable to heat at acid pH values (no loss of activity after 15 min at 80 °C). Has a molecular weight of ca. 13000 and is similar to ribonuclease both in size and in its remarkable stability to various denaturing agents
3.6.1.9 <i>Nucleotide pyrophosphatase</i> ⁸	Kidney, liver	ca. 8	Hydrolyses dinucleotides to give 2 mononucleotides	Acts rapidly on NADH ₂ , NADPH ₂ , FAD, adenosine diphosphate ribose and several analogues of NADH ₂ . The animal enzyme generally splits NADH ₂ faster than NAD. The enzyme from potato also splits ADP, ATP and thiamine pyrophosphate

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386).

References

¹ STADTMAN, T.C., in BOYER et al. (Eds.), *The Enzymes*, 2nd ed., vol. 5, Academic Press, New York, 1961, page 55.

² SCHMIDT, G., in BOYER et al. (Eds.), *The Enzymes*, 2nd ed., vol. 5, Academic Press, New York, 1961, page 37.

³ ASHMORE and WEBER, *Vitam. and Horm.*, 17, 91 (1959).

⁴ CORI and CORI, *J. biol. Chem.*, 199, 661 (1952).

⁵ MOKRASCH and MCGILVER, *J. biol. Chem.*, 221, 909 (1956).

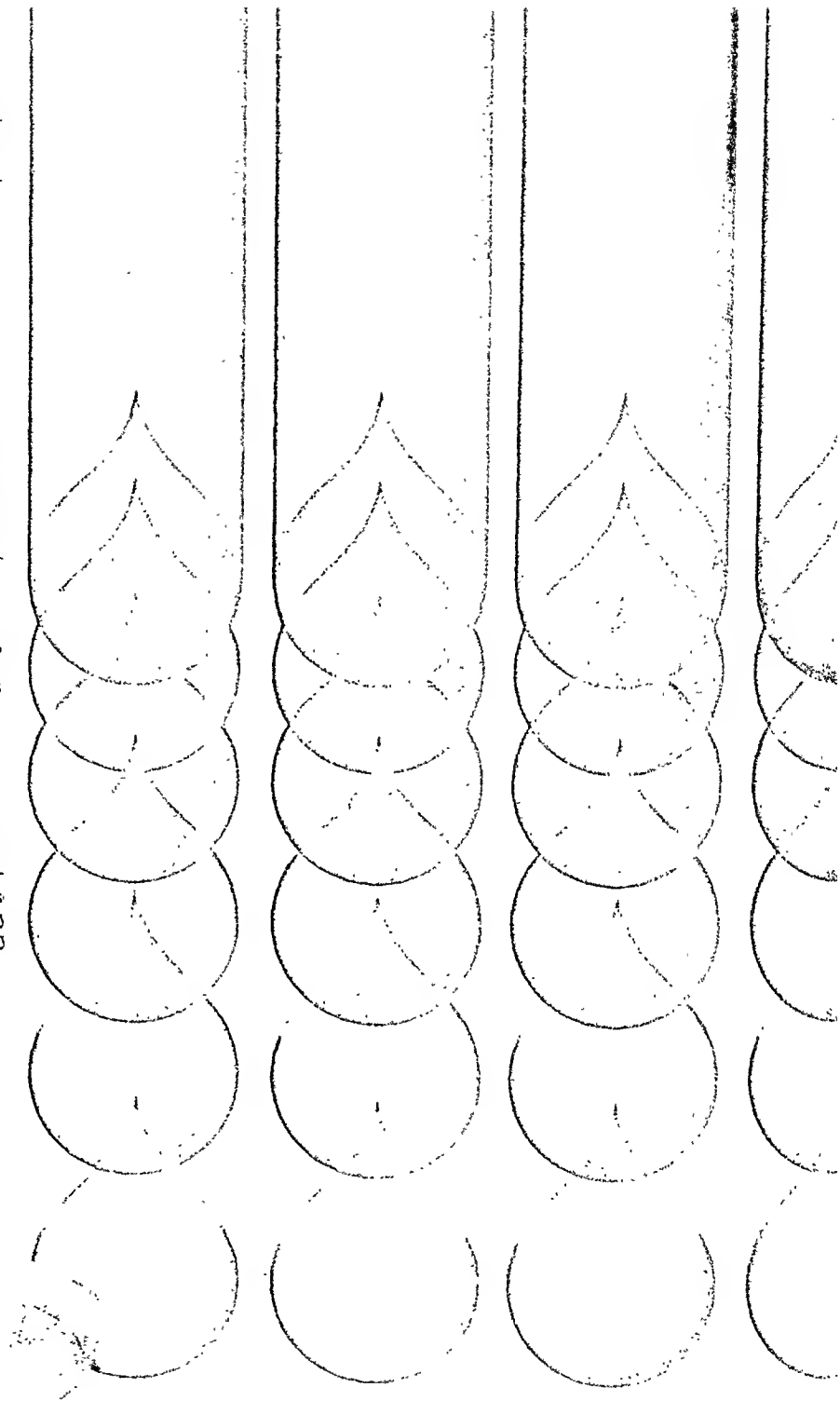
⁶ SEAL and BINKLEY, *J. biol. Chem.*, 228, 193 (1957).

⁷ RAJMAN et al., *J. biol. Chem.*, 235, 2340 (1960).

⁸ JACOBSON and KAPLAN, *J. biophys. biochem. Cytol.*, 3, 31 (1957).

Table 15 (continued) Phosphatase

Enzyme*	Location
3.1.4 Phosphodiesterases	Widespread
3.6.1.1 Inorganic pyro- phosphatase ⁶	Liver, brain, erythrocytes other tissues
3.6.1.7 Acylphosphatase ⁷	Skeletal mus- cle, brain, kidney liver, leucocytes
3.6.1.9 Nucleotide pyro- phosphatase ⁸	



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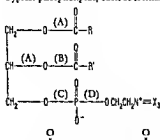
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16 Phospholipases

Typical phospholipids, such as lecithin or cephalin, may be represented by the general formula



where R-C-O is a saturated, R'-C-O- an unsaturated, long chain fatty acid, X-CH₃ for lecithin, H for cephalin. The corresponding enzymes capable of cleaving the four designated bonds in the formula are called phospholipases A, B, C and D. Since the term "lipase" usually refers to the cleavage of a carboxyl ester, phospholipases C and D are in a strict sense phosphodiesterases.

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
14 phospholipase A ¹	Muscle, heart, liver, kidney, adrenals, pancreas	ca 7		without loss of activity. Cleaves the phospholipid-cytochrome complex within mitochondria, causing powerful inhibition of certain respiratory enzymes
15 phospholipase B ¹ (lysophospholipase)	Liver, pancreas	4.0-6.0		
143 phospholipase C	<i>Clostridium</i> toxins, brain ²	6.0-7.6		Stable, retains 50% of its activity after heating at 100°C for 10 min
144 phospholipase D	Not present in mammalian tissues. Found in plants ²	5.1-5.9	Cleavage of the phospholipid at the point marked (D) in the formula	Catalyses hydrolysis of glycerol phosphorylcholine, produced by the joint action of phospholipase A and B, to glycerol phosphate and choline. Resembles phospholipase D in specificity. Also acts on glycerophosphoethanolamine. Requires Mg ⁺⁺ . The enzyme has been purified from bacterial extracts
142 Necrophosphatidyl choline diesterase	Nervous tissue ¹ , liver and other tissues ²	7.5-9.0		

The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 386)

References

1. Sorsa K H
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3. ...
4. ...
5. ...

Table 17 Nucleases and other enzymes acting on nucleotides and nucleosides

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
2.7.7.16 <i>Ribonuclease</i> ¹ (RNAase)	Most tissues, highest activity in the pancreas <i>RNAase content of vertebrate pancreas (µg/g)</i> ¹¹ Cow 1200 Sheep 1080 Goat 1000 Mouse 395 Lizard 380 Rat 260 Guinea-pig 240 Pig 80 Horse 25 Chicken 20 Whale 18 Monkey 2 Man 1 Cat 0.5 Dog 0.5 Rabbit 0.5	7.0-8.0	Catalyses the depolymerization of ribonucleic acid, producing nucleoside 3'-phosphates. The animal enzymes cannot attack purine nucleoside phosphate linkages and consequently produce a resistant 'core' rich in purine bases	First action of RNAase on internucleotide bonds is transesterification to form a pyrimidine nucleoside cyclic 2',3'-phosphate ester. These terminal groups are split off as free mononucleotide cyclic phosphates which are then hydrolysed with the formation of the corresponding nucleoside 3'-phosphates. Some enzymes produce nucleoside 5'-phosphates from RNA. Bovine pancreatic RNAase has been extensively studied
3.1.4.5 <i>Deoxyribonuclease</i> ² (DNAase) 3.1.4.6 <i>Deoxyribonuclease II</i> ² (DNAase II)	Many tissues, pancreas being the best source	ca. 7 4.5-5.5	Catalyse the depolymerization of deoxyribonucleic acids. Products include mononucleotides through to oligonucleotides. All four mononucleotides have been isolated from the enzyme digests. The nucleotides are terminated in 5'-phosphates in the case of DNAase and 3'-phosphates in the case of DNAase II	DNAase requires added Mg ⁺⁺ for activity, is inhibited by EDTA and has a pH optimum at ca. 7. DNAase II is inhibited by added Mg ⁺⁺ , often activated by EDTA and has a pH optimum at pH 4.5-5.5. Both DNAases can occur in the same tissue
3.1.4.1 <i>Phosphodiesterase</i> ³	Intestine, spleen and other tissues	ca. 7	Hydrolyses phosphoric diesters to give a phosphoric monoester and an alcohol	Attacks both ribo- and deoxyribo-internucleotide bonds. Has wide specificity. The spleen enzyme forms 3'-nucleotides
3.1.3.5 <i>5'-Nucleotidase</i> ⁴	Retina, nervous tissue, prostate, testes, sperm. In human tissues the highest activity is in the posterior pituitary gland	ca. 8	Hydrolyses all ribonucleoside and deoxyribonucleoside 5'-phosphates as well as nicotinamide mononucleotide to the corresponding nucleosides and orthophosphate	Preparations of the enzyme, especially from snake venom and bull seminal plasma, have been used to help establish the identity of nucleoside 5'-phosphates
2.4.2.1 <i>Purine nucleoside phosphorylase</i> ⁵	Liver, brain, thymus, erythrocytes and other tissues	ca. 7	Pentose 1-phosphate + purine \rightleftharpoons nucleoside + orthophosphate	Since the reaction is readily reversible the enzyme is often assayed as orthophosphate released on nucleoside formation. At least two classes of enzymes, purine and pyrimidine nucleoside phosphorylases, have been recognized. The specificity of the various enzymes has not been completely determined. It seems likely that these enzymes play a role in nucleic acid breakdown rather than in nucleoside synthesis

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385-386).

Table 17 (continued) Nucleases and other enzymes acting on nucleotides and nucleosides

Enzyme*	Location	Optimal pH of action	Reaction catalysed	Remarks
3546 <i>AMP deaminase</i> ⁸	Muscle and other tissues	6.1-6.4	Deaminates adenylic acid to inosinic acid and ammonia	Acts only on 5'-adenylic acid and 5'-deoxyadenylic acid. The rate with the latter is about 1% of that with the former
3544 <i>Adenosine deaminase</i> ⁸	Muscle, liver, intestinal mucosa	ca. 7.5	Deaminates adenosine to inosine and ammonia	Deoxyadenosine is also deaminated
3543 <i>Guanine deaminase</i> ^{8,9}	Liver, muscle	6-10	Deaminates guanine to xanthine and ammonia	to determine micro-amounts of guanine
1232 <i>Xanthine oxidase</i> ⁸	Milk, liver, spleen, kidney, lung	7.4	The purified enzyme oxidizes hypoxanthine to xanthine, xanthine to uric acid, and aldehydes to acids	Contains flavin adenine dinucleotide, iron and molybdenum
1733 <i>Urate oxidase</i> ¹⁰	Liver and kidney of mammals. Absent in man and other primates	9.2	Oxidizes uric acid to allantoin according to the overall reaction: $\text{uric acid} + \text{O}_2 + 2\text{H}_2\text{O} \rightarrow \text{allantoin} + \text{H}_2\text{O}_2 + \text{CO}_2$	Contains copper. The production of allantoin is dependent on the interaction of the reaction intermediates with the buffer ions. In phosphate and tris buffers the product is allantoin alone but in borate buffer only 30% of the product is allantoin

* The numbers and trivial names are those recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385 and 3465).

⁸ FAZELLE, W. E., in GOLDBECK and KARLAN (Eds.), *Methods in Enzymology*, vol. 6, Academic Press, New York, 1963, page 236.

References

- ¹ ASPERSEN and WHITE, in BOYER et al. (Eds.), *The Enzymes*, 2nd ed., vol. 5, Academic Press, New York, 1961, page 95.
² LASHOWSKI, M., in BOYER et al. (Eds.), *The Enzymes*, 2nd ed., vol. 5, Academic Press, New York, 1961, page 123.

Synthesis of cell constituents

Apart from supplying energy, the products of digestion serve as precursors of many cell constituents. The mammalian body can form all cell constituents from:

1. The essential amino acids (see page 434)
2. Vitamins
3. The essential (highly unsaturated) fatty acids
4. Mineral salts
5. A bulk source of carbon (usually carbohydrate)
6. A source of nitrogen in the form of ammonia derived mainly from surplus amino acids, with small amounts supplied by purine bases, pyrimidines and amino sugars.

Carbohydrate as a bulk source of carbon can be largely replaced by protein and fat, especially in carnivores.

Much progress has been made in recent years in the elucidation of the pathways by which the basic constituents of food are converted into cell constituents, but many details still remain to be clarified. A synopsis of the available information is contained in this section which follows.

Synthesis of cell constituents from glucose

The principal products, their pathways of formation and their physiological functions are summarized in Table 18 below.

The oxidative pentose phosphate cycle

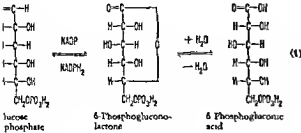
Glucose 6-phosphate (formed from glucose by the hexokinase reaction) can be oxidized in liver and some other animal tissues at the carbon atom 1 to yield 6-phosphogluconate. This initiates a sequence of reactions in which various pentose phosphates and other sugar phosphates are formed. In the course of these reactions

Table 18 Formation of basic cell constituents and metabolites from glucose

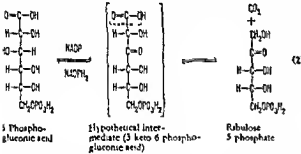
Product formed	Pathway of formation	Physiological function
Glycogen	From glucose 1-phosphate via UDP-glucose, catalysed by UDPG pyrophosphorylase and UDPG glycogen glucosyltransferase ¹	Storage of carbohydrate
Galactose	Reversal of reactions 4 and 5, Table 4, page 390	Constituent of lactose, cerebroside
Lactose	Probably from UDP-galactose and glucose 1-phosphate, via lactose 1-phosphate	Milk constituent
Ribose 5-phosphate	Reactions of the pentose phosphate cycle (see opposite page)	Constituent of nucleic acid and nucleotides
Deoxyribose 5-phosphate	Probably by aldol condensation between glyceraldehyde phosphate and acetaldehyde (reversal of the reaction shown on page 399)	Constituent of nucleic acids
Glucuronic acid and iduronic acid	Formed via UDP-glucose (see page 423)	Constituent of mucins (hyaluronic acid and chondroitin sulphate) and of heparin; detoxicating agent
Glucosamine	From fructose 6-phosphate by transfer of the amido group of glutamine (see page 423)	Constituent of lipids, polysaccharides and glycoproteins
L-Fucose	From fructose 6-phosphate via GDP-mannose (see page 423)	Constituent of milk oligosaccharides and glycoproteins
Fructose	Reactions of glycolysis and hydrolysis of fructose 6-phosphate by phosphatase	Constituent of semen
Citric acid	CO ₂ -fixation by pyruvate (see page 424) and reactions of the tricarboxylic acid cycle (see page 390)	Constituent of bone, milk, semen
Fatty acids	From acetyl-coenzyme A (formed via pyruvate) by a route involving malonyl-coenzyme A	Constituents of fats and phospholipids
Glycerophosphates	Reduction of dihydroxyacetone phosphate, catalysed by glycerophosphate dehydrogenase	Constituents of phospholipids
Phospholipids	See page 425	Cell constituents
Glyceride fats	See page 426	Cell constituents
Sterols and steroids	See pages 426-432	Cell constituents; hormones
Nonessential amino acids:		
Glutamic acid	Glutamate dehydrogenase reaction (see page 432)	Constituent of proteins and special peptides (glutathione, folic acid)
Aspartic acid	CO ₂ -fixation by pyruvate (see page 424) and transamination between glutamate and oxaloacetate	Constituent of proteins
Alanine	Transamination between pyruvate and glutamate	Constituent of proteins
Glycine	From 3-phosphoglycerate by the reactions shown on page 432	Constituent of proteins
Serine		Constituent of proteins
Cysteine	From serine by transsulphuration from homocysteine derived from methionine (see pages 397-398)	Constituent of proteins
Proline	From glutamic acid or ornithine (see page 432)	Constituent of proteins
Hydroxyproline	Probably by oxidation of proline (see page 432)	Constituent of proteins

the glucose 6-phosphate is regenerated, implying a cyclic nature of the reaction sequence. The reactions of this cycle represent a

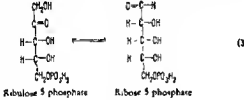
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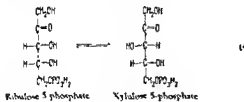
The 6-phosphogluconate formed is oxidatively decarboxylated (1) to yield ribulose 5-phosphate, while another molecule of NADP is reduced.



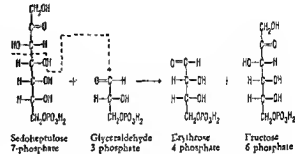
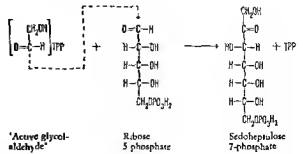
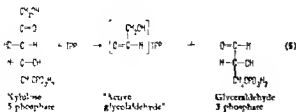
Ribulose 5-phosphate undergoes two different isomerizations, one to ribose 5-phosphate (3) catalysed by pentose phosphate isomerase.



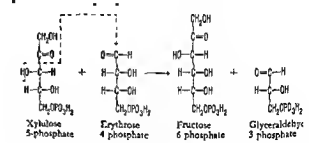
and one (4) to xylulose 5-phosphate.



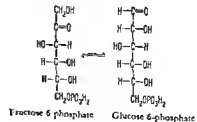
This may therefore be written as



The reaction (6) is:



The fructose 6-phosphate formed in reactions (6) and (7) is converted to glucose 6-phosphate by reaction (8), catalysed by glucose phosphate isomerase.



This reaction completes the cycle in that it leads to the (partial) regeneration of the starting material, glucose 6-phosphate. The interplay of the components of the cycle is somewhat complex as shown diagrammatically in Figure 11 and Table 19 (page 4).

In this scheme, the reactions catalysed by transketolase (5), (6) and (7) are indicated by dashed lines.

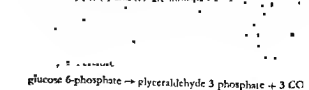


Table 19 The component reactions of the pentose phosphate cycle and their quantitative relations

(1)	3 glucose 6-phosphate + 3 NADP	(glucose 6-phosphate dehydrogenase)	3 6-phosphogluconate + 3 NADPH ₂
(2)	3 6-phosphogluconate + 3 NADP	(phosphogluconate dehydrogenase)	3 ribulose 5-phosphate + 3 CO ₂ + 3 NADPH ₂
(3)	ribulose 5-phosphate	(ribosephosphate isomerase)	ribose 5-phosphate
(4)	2 ribulose 5-phosphate	(ribulosephosphate 3-epimerase)	2 xylulose 5-phosphate
(5)	ribose 5-phosphate + xylulose 5-phosphate	(transketolase)	sedoheptulose 7-phosphate + glyceraldehyde 3-phosphate
(6)	sedoheptulose 7-phosphate + glyceraldehyde 3-phosphate	(transaldolase)	fructose 6-phosphate + erythrose 4-phosphate
(7)	xylulose 5-phosphate + erythrose 4-phosphate	(transketolase)	fructose 6-phosphate + glyceraldehyde 3-phosphate
(8)	2 fructose 6-phosphate	(glucosephosphate isomerase)	2 glucose 6-phosphate
Sum	glucose 6-phosphate + 6 NADP		3 CO ₂ + glyceraldehyde 3-phosphate + 6 NADPH ₂

Fig. 11 Diagram of the pentose phosphate cycle

Starting materials and end-products are shown enclosed. P = phosphate. The crossing arrows indicate transfer reactions. For further details see Table 19 and the text.

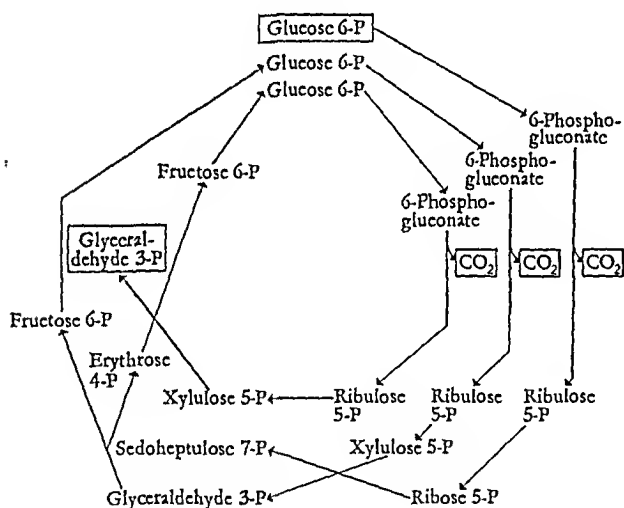
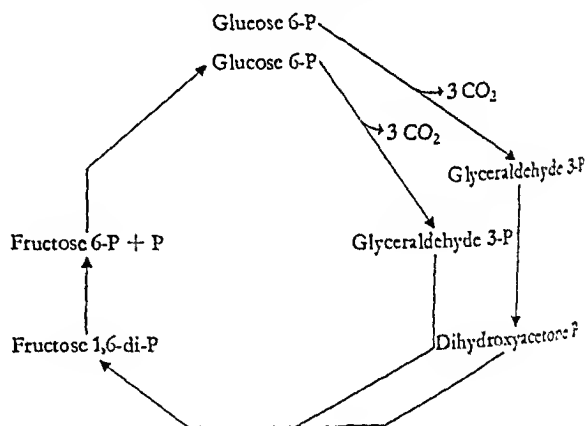
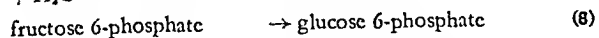
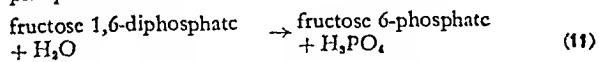
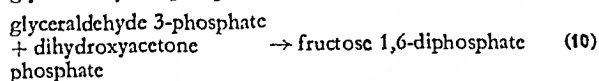
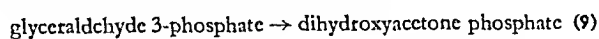


Fig. 12 Complete oxidation of glucose 6-phosphate via the pentose phosphate cycle and additional reactions catalysed by triosephosphate isomerase, fructose-1,6-bisphosphate aldolase, hexosediphosphatase and glucosephosphate isomerase

The first step shown in the diagram (conversion of glucose 6-phosphate into glyceraldehyde phosphate + 3 CO₂) represents the sum of the reactions shown in Table 19 and Figure 11. P = phosphate



The glyceraldehyde 3-phosphate thus formed does not, however, accumulate in the organism. It can be converted into pyruvate and acetyl-coenzyme A and undergo complete oxidation. Alternatively, if triosephosphate isomerase, fructose-1,6-bisphosphate aldolase, hexosediphosphatase and glucosephosphate isomerase are present, the following sequence of reactions can occur:



Glucose 6-phosphate would thus be formed from two molecules of glyceraldehyde 3-phosphate, and could re-enter (and be oxidized by) the pentose phosphate cycle. Reactions (1)-(11) repeated several times would therefore result in a complete combustion of glucose 6-phosphate. This concept, which rests on the demonstration of all the required enzymes in liver¹¹, is illustrated in Figure 12.

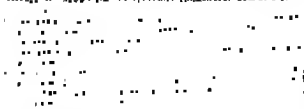
Physiological significance of the oxidative pentose phosphate cycle. The oxidative pentose phosphate cycle is not a major source of energy. Its function is probably twofold: to supply (1) pentose phosphates required for the synthesis of nucleic acids, and (2) reduced NADPH required as a source of hydrogen in many reductive syntheses. Quantitatively, the most important reductive synthesis in animal tissues is the formation of fatty acids from carbohydrates, and this is in accordance with the fact that the activity of the enzymes of the pentose phosphate cycle is particularly high at the sites of lipogenesis, for instance in the lactating mammary gland and in adipose tissue¹².

References

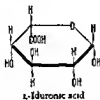
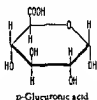
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Metabolism - Synthesis of Cell Constituents from Glucose

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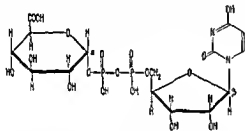
Glucuronic acid and Iduronic acid



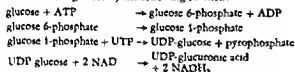
D-Glucuronic acid and L-iduronic acid are components of mucopolysaccharides, such as the chondroitin sulphates. Glucuronic acid is also a coupling agent in detoxication reactions. It couples

and with bile pigments?

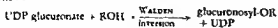
The reactive form of glucuronic acid in the conjugation reactions, in the synthesis of mucopolysaccharides and in the interconversion of glucuronic and iduronic acids is UDP-glucuronic acid.



This arises from glucose by the following reactions? *



The synthesis of conjugated glucuronide may be represented as follows:



where ROH is an alcoholic or phenolic compound, or an aromatic carboxylic acid.

UDP-glucuronic acid is converted to uridine diphosphoglucuronic acid by an epimerase that attacks the 5-position of the sugar ring. NAD acts catalytically.

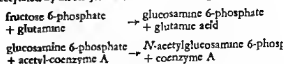
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1. WILLIAMS R.T., *Detoxication Mechanisms*, 2nd ed., Chapman & Hall, London, 1969.
2. BILLING et al. *Biochem J.*, 65, 774 (1957).
3. NYSTROMER et al. *J. Amer. chem. Soc.*, 76, 6411 (1954).
4. JACOBSON and DAVIDSON, *J. Biol. Chem.*, 237, 635 (1962).
5. SMITH and MILES, *Biochim. biophys. Acta (Amst.)*, 13, 386 (1954). STORSTAD and DAVIES, *Biochem J.*, 59, 279 (1955).

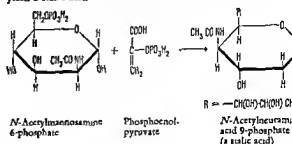
Formation of glucosamine and related amino sugars

Glucosamine, mannosamine, and their N-acetyl derivatives, as well as sialic acid, occur in lipids, polysaccharides and glycoproteins. Glucosamine is formed from fructose 6-phosphate by

transfer of the amido group of glutamine. The amino sugar is acetylated by an enzymatic reaction involving acetyl-coenzyme

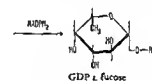
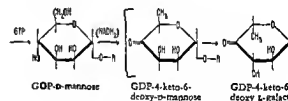
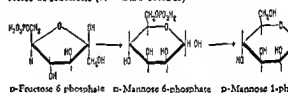


The sugar N-acetylglucosamine is converted to N-acetylmannosamine, which is then phosphorylated with ATP to yield a phosphate derivative. This reacts with phosphoenolpyruvate to yield a sialic acid.

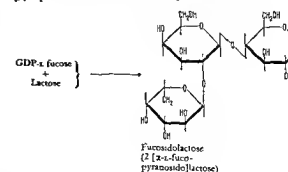


Biosynthesis of L-fucose in mammalian tissues

L-Fucose is formed from fructose 6-phosphate by the following series of reactions (R = GDP residue)



Incorporation of L-fucose into milk oligosaccharides and glycoproteins is via GDP-L-fucose.

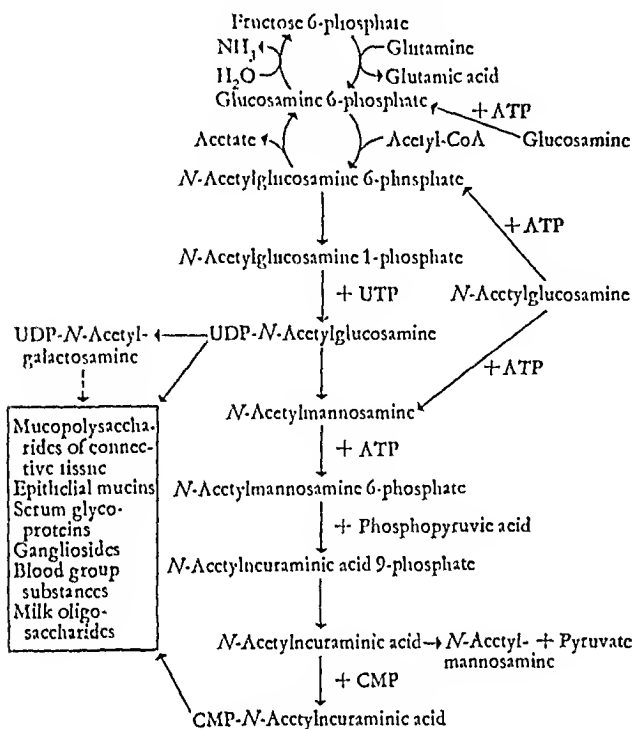


Reference

1. ...
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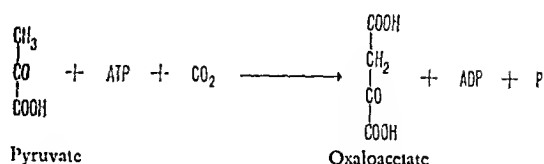
Formation and utilization of hexosamines and *N*-acetylneuraminic acid in mammals

The following scheme illustrates the manner in which these amino sugars¹ are formed and utilized in the mammalian organism:



References

- 1 On amino sugar metabolism in general see WOLSTENHOLME and O'CONNOR (Eds.), *Ciba Foundation Symposium on the Chemistry and Biology of Mucopolysaccharides*, Churchill, London, 1958; ROSEMAN, S., *Ann. Rev. Biochem.*, 28, 545 (1959); GOTTSCHALK, A., *The Chemistry and Biology of Sialic Acids and Related Substances*, Cambridge University Press, London, 1960; WHITEHOUSE and ZILIKEN, *Meth. biochem. Anal.*, 8, 199 (1960); CLARK and GRANT (Eds.), *The Biochemistry of Mucopolysaccharides of Connective Tissue*, Biochem. Soc. Symp., No. 20 (1961); STACY and BARKER, *Carbohydrates of Living Tissues*, Van Nostrand, London, 1962; MCGARRAHAN and MALEY, *J. biol. Chem.*, 237, 2458 (1962); SPIRO, R.G., *New Engl. J. Med.*, 269, 566 (1963); Symposium on Mucous Secretions, *Ann. N.Y. Acad. Sci.*, 106, 157 (1963); BRIMACOMBE and WEBBER, *Mucopolysaccharides*, Elsevier, Amsterdam, 1964; DORFMAN, A., *Biophys. J.*, 4, suppl., 155 (1964); GINSBURG, V., *Advanc. Enzymol.*, 26, 35 (1964); GRANT and SIMKIN, *Ann. Rev. chem. Soc.*, 61, 491 (1964); KORNFIELD et al., *Proc. nat. Acad. Sci. (Wash.)*, 52, 371 (1964); SARCIONE, E.J., *J. biol. Chem.*, 239, 1686 (1964); CARTER et al., *Ann. Rev. Biochem.*, 34, 109 (1965); MOLNAR et al., *J. biol. Chem.*, 240, 1882 (1965); JEANLOZ and BALAZS (Eds.), *The Amino Sugars*, 2 vols., Academic Press, New York, 1965/66; GOTTSCHALK, A., *Glycoproteins*, Elsevier, Amsterdam, 1966.



Both reactions readily occur in liver tissue and also elsewhere. They are reversible. The malic and oxaloacetic acids form enter the tricarboxylic acid cycle and form citrate and a glutarate.

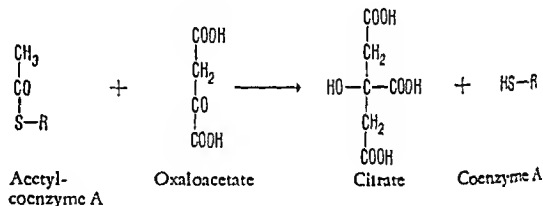
References

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- 2 UTTER and KRECH, *J. biol. Chem.*, 238, 2603 (1963).

Fatty acid synthesis

Acetyl-coenzyme A formed from carbohydrate or amino acid if not required for energy supply or special biosyntheses, can be converted to fatty acids. Most of the acetyl-coenzyme A is formed within the mitochondria, but the synthesis of fatty acids is an extramitochondrial process¹. Acetyl groups must therefore be derived from the mitochondria to the extramitochondrial space. This requires a special mechanism since acetyl-coenzyme A as such cannot diffuse into or out of the mitochondria². The acetyl group is probably transferred as follows³:

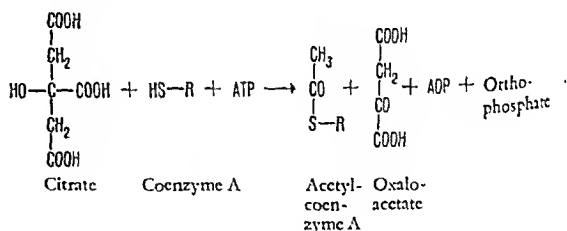
Formation of citrate (intramitochondrial)



Diffusion

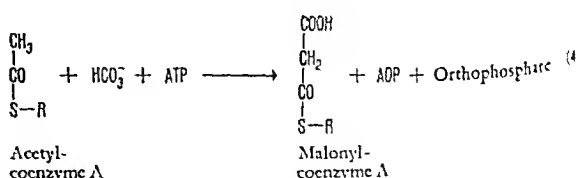
Intramitochondrial citrate \rightarrow extramitochondrial citrate

Cleavage of citrate (extramitochondrial)

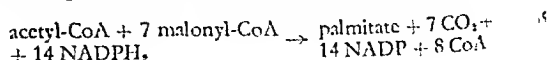


It is to be noted that reactions (1) and (3) are catalysed by different enzymes⁴. Reaction (3) is followed by the carboxylation of acetyl-coenzyme A to yield malonyl-coenzyme A⁵:

Acetyl-coenzyme A carboxylase reaction

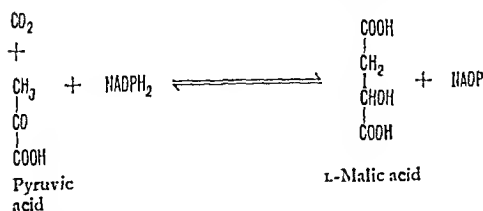


The enzyme catalysing this reaction contains biotin and requires citrate as an activator. Acetyl-coenzyme A and malonyl-coenzyme A then condense and are reduced according to the following stoichiometric equation⁶:



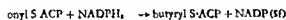
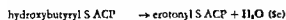
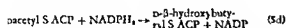
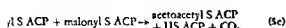
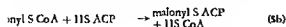
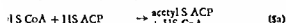
Extension of carbon chains by carbon dioxide fixation

An important link in the building-up of the carbon skeletons of cell constituents is the addition of CO_2 to pyruvate. There are at least two CO_2 -fixation reactions in animal tissues by which 4-carbon chains arise from pyruvate. The first¹ is catalysed by the 'malic' enzyme; it requires reduced NADP and leads to L-malic acid:



The second reaction requires ATP and consists of the carboxylation of pyruvate to oxaloacetate, catalysed by the enzyme pyruvate carboxylase²:

action is catalysed by a cytoplasmic enzyme complex² con- of at least 6 or 7 different kinds of protein; these are tightly together in yeast and pigeon liver but readily dissociable in ind several plant systems. An 'acyl carrier protein' (ACP) n isolated from *E. coli* which binds acyl intermediates during mation of long-chain fatty acids. ACP contains one free dryl group per molecule, derived from 2-mercaptoethyl- which binds the acyl derivative to form a thioester³. The ual steps of the fatty acid synthesis in *E. coli* are as follows



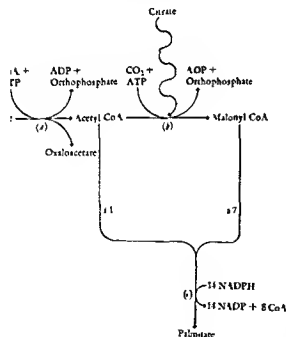
ryl S ACP then undergoes condensation with another mole-



palmityl group of palmityl CoA may then be hydrolysed to late or transferred to α -glycerophosphate and related com- is (3), (4) and (5) of this process are summarized in Figure 13

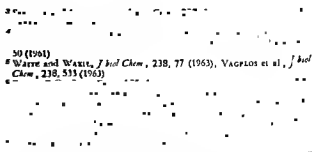
3 Fatty acid synthesis from citrate

(a) Citrate cleavage enzyme (b) Acetyl Coenzyme A carboxylase (activated by citrate) (c) 1 enzyme complex



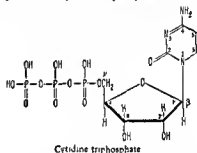
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 CHASTIN, J M., in GRAY, J K. (Ed.), *The Control of Lipid Metabolism*, Academic Press, New York, 1963, page 57. FARRE and JAY, *Am J Biol*, 206-231 (1964)



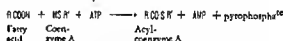
Formation of lecithin and cephalin

The synthesis of lecithin in animal tissues from fatty acids, glyc- erophosphate and choline requires the participation as cofactors of ATP, coenzyme A and cytidine triphosphate,

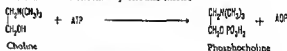


The intermediary stages of the synthesis are as follows.

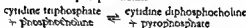
(a) 'Activation' of fatty acids¹



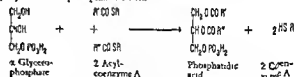
(b) 'Activation' of choline by choline kinase²



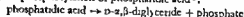
(c) 'Activation' of phosphocholine³



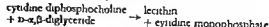
(d) Synthesis of phosphatidic acid³



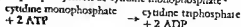
(e) Dephosphorylation of phosphatidic acid³



(f) Synthesis of lecithin³



(g) Rephosphorylation of cytidine monophosphate⁴



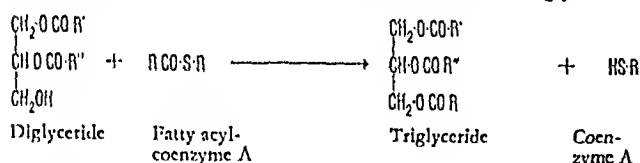
Cephalin is synthesized by analogous reactions, choline being replaced by ethanolamine ($\text{HO CH}_2\text{CH}_2\text{NH}_2$)

References

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2. WATSON, J. D., *Rev Biochem*, 31, 369 (1962).
3. WATSON, J. D., *Rev Biochem*, 31, 369 (1962).
4. WATSON, J. D., *Rev Biochem*, 31, 369 (1962).

Formation of triglyceride¹

The synthesis of triglyceride requires α -glycerophosphate. Two molecules of fatty acyl-coenzyme A condense with α -glycerophosphate to form phosphatidic acid, and then diglyceride, as described in the previous section. The final step is the reaction of diglyceride with another molecule of fatty acyl-coenzyme A to form triglyceride:



References

- ¹ STEIN and SHAPIRO, *Biochim. biophys. Acta (Amst.)*, 24, 197 (1957); STEINBERG et al., *J. Biol. Chem.*, 236, 1631 (1961).

Biosynthesis of cholesterol¹

Cholesterol² is by far the commonest sterol of the animal kingdom, though related sterols, notably Δ^7 -sterols, are found to predominate in some primitive molluscs and starfish. Cholesterol is synthesized in almost all vertebrate tissues but most actively in the liver, intestine, adrenals and gonads. Synthesis does not take place in erythrocytes, and is reduced to extremely low levels in nerve and brain after myelination is completed. An important function of cholesterol is as a component of cell membranes and subcellular membrane structures, in which it is associated with phospholipids, glycolipids and proteins. The most likely type of interrelationship of these different components in membranes has been deduced from studies of the structure and composition of the myelin sheath and the erythrocyte membrane.

The rate of endogenous cholesterol synthesis is variable and in man has been estimated to range between 0.5 and 2 g per day²¹. The principal catabolic pathway for cholesterol is conversion to bile acids by the liver²². Some intact cholesterol leaves the body by excretion into the bile and some by direct loss through the intestinal wall and faeces. In the intestine some cholesterol is metabolized to coprosterol and coprostanone. A small proportion of the total cholesterol synthesized functions as a precursor of the steroid hormones of the adrenal cortex and of the steroid sex hormones.

The pathway of synthesis of cholesterol^{2,4} has been studied primarily in the rat. Certain important reaction steps⁵ have been studied *in vitro* with enzymes isolated from yeast, which synthesizes the related sterol, ergosterol. All the evidence assembled so far points to a unified mechanism of synthesis for the basic structure of all sterols. The sterols of plants (e.g., β -sitosterol) and fungi (e.g., ergosterol) differ from cholesterol in having extra carbon atoms in the side chain. These carbon atoms are added at a late stage in the synthesis by a mechanism so far not completely elucidated⁶.

The individual steps in the biosynthesis of cholesterol as understood at present are as follows (Fig. 14 opposite):

The molecule is built up from acetate units which condense in the form of their coenzyme A derivatives; the first condensation yields acetoacetyl-coenzyme A (I), the second involves the further condensation of this compound with a third acetyl-coenzyme A molecule to give hydroxymethylglutaryl-coenzyme A (II). For several years it was recognized that by some mechanism this product must yield a five-carbon 'isoprenoid' fragment which forms the basis of the sterol structure, but it was only with the discovery of mevalonic acid (III) and the subsequent study of its conversion to sterol⁷ that the details of this mechanism could be clarified. Hydroxymethylglutaryl-coenzyme A (II) is now known to be reduced by an NADP-dependent enzyme system to mevalonic acid (III). The occurrence of an aldehydic intermediate in this reduction is not certain. Mevalonic acid next undergoes at least two sequential phosphorylations yielding in turn mevalonic phosphate (IV) and mevalonic pyrophosphate (V), the phosphate group at each step being derived from a molecule of ATP. A third molecule of ATP is consumed in the next reaction, in which mevalonic pyrophosphate (V) undergoes both dehydration and decarboxylation to isopentenyl pyrophosphate (VII)⁸. This transformation probably involves the intermediate formation of the triphosphate (VI), but this compound has not been identified.

An isomerase converts the isopentenyl pyrophosphate (VII) to its dimethylallyl isomer⁹ (VIII), and a condensation reaction be-

tween dimethylallyl pyrophosphate and isopentenyl pyrophosphate now takes place to give geranyl pyrophosphate (IX). This compound in turn condenses with a further dimethylallyl pyrophosphate molecule to give farnesyl pyrophosphate¹⁰ (X). Each of these condensations takes place with elimination of the pyrophosphate group as the inorganic ion and the formation of a new double bond lying in the main chain allylic to the remaining pyrophosphate group. The steps probably involved in the first of these reactions are shown (VII + VIII). The second condensation (IX + VIII) follows by an analogous mechanism.

In some manner as yet undetermined, two molecules of farnesyl pyrophosphate condense to form the C_{30} triterpenoid hydrocarbon squalene (XI). This condensation is known to involve stereospecific addition of hydrogen from reduced NADP¹¹. Squalene now undergoes a series of ill-defined cyclization and rearrangement reactions ending in lanosterol¹² (XII), with 2,3-oxidosqualene as intermediate²³.

Comparison of the structures of lanosterol (XII) and cholesterol (XIX) shows that the remaining biosynthetic steps must involve the removal of three methyl substituents from the 4 α -, 4 β - and 14 α -positions of lanosterol. Other necessary changes are the saturation of the double bond in the side chain and the conversion of the Δ^4 - to the Δ^5 -nuclear structure. The three 'extra' methyl groups appear to be removed prior to the other changes in the molecule. In the pathway operating in the rat, the 14 α -methyl group is removed first¹³ and the two methyl substituents in position 4 are then removed in turn. The carbon atoms detached from the nucleus in these reactions are converted to CO_2 ¹⁴ and the oxidation of each methyl to a carboxylic acid group seems likely to occur in each case. The final decarboxylation step is thought to be facilitated in the case of the 14 α -methyl group by the proximity of the Δ^4 -bond and in the case of the C $_4$ -methyl groups by the transitory oxidation of the 3 β -OH group to a ketone. Evidence for the latter step is the fact that the loss of the 4 α -methyl group takes place with exchange of the 3 α -hydrogen atom (demonstrated with 3 α -tritium labelled substrates)¹⁵.

The demethylation steps, if they occurred with no other changes in the molecule, would lead to the formation of Δ^4 , Δ^5 -cholestadienol-(3 β) (zymosterol) (XV). This compound is known as a minor sterol of yeast and evidence for its participation in the biosynthesis of cholesterol in the rat has been given¹⁶. The steps involved in the conversion of the Δ^4 -structure of zymosterol to the Δ^5 -structure of cholesterol are still unclear at many points. It seems likely that the Δ^4 -bond is shifted to Δ^5 by some 'direct' mechanism involving hydrogen transfer. The conversion of Δ^4 -cholestenol-(3 β) to cholesterol probably takes place via the Δ^3 -derivative and is known to require oxygen, but the participation of a 6-hydroxylated derivative has not been demonstrated.

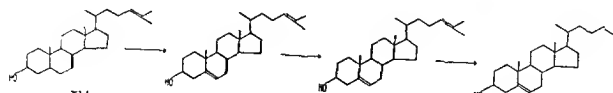
It has been suggested that in rat liver the conversion of zymosterol to cholesterol takes place via the Δ^7 , Δ^8 , Δ^5 , Δ^7 , Δ^8 , and Δ^5 , Δ^7 , Δ^8 , Δ^9 intermediates (XVI-XVIII) respectively, with the final step in the biosynthesis of cholesterol involving reduction of the Δ^9 -bond⁴. The Δ^5 , Δ^7 -sterol desmosterol (XVIII), known to occur naturally in trace amounts in adult mammalian tissues¹⁷ and in larger amounts in embryonic chick tissues¹⁸, accumulates in the liver of rats treated with the anticholesterologenic drug triparanol¹⁹. However, the question of whether the Δ^9 -bond is retained until the last step in cholesterol synthesis must be regarded as unsettled at the present time. Evidence presented by several laboratories indicates that all the conversions from lanosterol onwards can be accomplished by enzymes of rat liver with substrates in which the Δ^9 -bond is either present or absent. Moreover, normal rat skin contains a complex mixture of sterols with a saturated side chain but with nuclear structures representing nearly all the possible stages in the conversion of lanosterol to cholesterol. Triparanol treatment leads to the accumulation of the Δ^9 -analogues of all these compounds in the skin²⁰. It is possible that there are differences between tissues that determine whether cholesterol biosynthesis takes place predominantly via the Δ^9 -series of compounds, including desmosterol (XVIII), or via the series of analogues in which the side chain is saturated, but whether it is necessary to envisage the process as occurring by one or the other of two mutually exclusive pathways is not clear.

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(continued on page 427)

Fig. 14 Biosynthesis of cholesterol



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Biosynthesis and metabolism of steroid hormones of the adrenal cortex and gonads (for references see page 430)

The normal adrenal cortex produces a wider variety of steroid hormones than either the ovary or the testis¹. Besides producing eight C₂₁-steroids of known structure and proven 'corticoid' activity, it also produces many C₂₁-steroids of unknown physiological activity as well as progesterone, the oestrogens and the androgens of the C₁₉, O₂- and C₁₉, O₃-series²⁻⁴. Adrenal androgen formation⁵ is at present more fully documented than the formation of adrenal oestrogens, and the pathway of testicular androgen formation appears to be clearly represented in the adrenal cortex. It is therefore convenient to outline the pathways of androgen synthesis together with the pathways of synthesis of C₂₁-steroids in a single scheme (Fig. 15), since these two aspects of steroid metabolism are closely interlinked. The oestrogenic steroids are further transformation products of the androgens and are more conveniently discussed separately (see page 430). The adrenal cortex, the testis, the ovary and the placenta are all capable of synthesizing their characteristic steroid hormones from acetate via cholesterol and pregnenolone, and it seems likely that most of the biosynthetic reactions involved in the synthesis of all classes of steroid hormones are possible in all the above-mentioned organs. However, it is not certain to what extent the hormones secreted normally in vivo are formed from acetate, from blood cholesterol or from steroid precursors synthesized in the adrenal cortex.

The C₂₁-corticoids have profound effects on carbohydrate and protein metabolism ('glucocorticoid' activity) and on sodium and potassium metabolism ('mineralocorticoid' activity). Most of these compounds exert effects of both types with one or the other predominating, according to their chemical structure. The more powerful glucocorticoids are those having oxygen functions at both C-11 and C-17. The glucocorticoid action of the human adrenal is considered to be accounted for almost wholly by the cortisol (hydrocortisone) it produces, since this is both the most potent naturally occurring steroid in this respect and also the most abundant product of the adrenal cortex in man. Corticosterone, the most abundant corticoid of the rat, has a less powerful glucocorticoid action. It is now clear that a portion of the cortisol or corticosterone output of the adrenal is in a protein-bound form in the blood⁶. It seems probable that the unbound portion is to be regarded as the physiologically active form, and various factors (for instance oestrogen levels) affecting the degree of protein-binding of the glucocorticoids may therefore exert important effects on their physiological function. The most potent hormone in the regulation of salt metabolism is aldosterone, a quantitatively minor product. Deoxycorticosterone has a much smaller but still detectable effect on salt metabolism. For further discussion of the adrenocortical steroids see pages 742 sq.

Figure 15 shows the most probable routes of biosynthesis of the physiologically active C₂₁-steroids of the adrenal and depicts the main pathways leading to the androgens testosterone, Δ⁴-androstenedione, dehydroepiandrosterone, 11β-hydroxy-Δ⁴-androstenedione and Δ⁴-androstene-3,11,17-trione (adrenosterone). All these C₁₉-steroids may arise in the adrenal but the last two, having 11-oxygen functions, are probably specifically products of the adrenals

Testosterone is certainly the principal androgen of the testis but probably is formed in only trace amounts in the adrenal. Both the testis and adrenal give rise to some Δ⁴-androstenedione and dehydroepiandrosterone (see page 751).

The pathways outlined in Figure 15 are largely based on evidence from *in vitro* work with adrenal and testis tissues, but the evidence of *in vivo* studies in man is consistent with the operation of these pathways. There is an extensive literature on steroid biosynthesis and metabolism in the adrenals and gonads in pathological states, especially in various types of tumours of these tissues and in abnormalities having a genetic basis. The major genetic abnormalities are briefly considered below, but metabolic studies with tumour tissues will not be discussed, though it should be noted that they frequently show abnormal biosynthetic patterns suggested by the symptoms to which the tumours give rise (for instance masculinizing adrenal tumours produce androgens; feminizing tumours produce oestrogens). Since such findings most probably represent an exaggeration of the normal biosynthetic potentialities rather than the addition of totally new features they provide valuable clues to the normal pathways of synthesis.

The C₂₁-steroids of the adrenals can all be derived from cholesterol via 20α-hydroxycholesterol and 20α,22E-dihydroxycholesterol. In the adrenals, the first identifiable C₂₁-steroid, pregnenolone, is mostly converted via progesterone into the more highly oxygenated C₂₁-corticoids. A minor pathway for pregnenolone in both the adrenals and testes involves its conversion to 17α-hydroxypregnenolone, which serves as a precursor of the weak androgen dehydroepiandrosterone. The conversion of progesterone into the C₂₁-corticoids takes place mainly by one of two divergent pathways depending upon whether hydroxylation takes place first at the 17α-position (giving 17α-hydroxypregesterone) or the 21-position (giving deoxycorticosterone). Most of the data indicate that hydroxylation at C-17 proceeds more readily in the absence of the 21-hydroxyl group⁷. Both deoxycorticosterone and 17α-hydroxydeoxycorticosterone may undergo hydroxylation at the 11β-position giving respectively corticosterone and cortisol, which on further oxidation at C-11 yield minor amounts of two further physiologically active substances, 11-dehydrocorticosterone and cortisone. The pathway to aldosterone is still not clear, but its formation from deoxycorticosterone by hydroxylation at C-18 to 18-hydroxycorticosterone and subsequent oxidation has been demonstrated. Other synthetic pathways are also possible⁸. The mechanisms by which aldosterone and cortisol output are controlled (see page 430) are markedly different and in this connection it is probably significant that aldosterone secretion seems to be almost exclusively confined to the outer zone (zona glomerulosa) of the cortex, cortisol secretion to the inner zones.

Further metabolism of C₂₁-steroids and the formation of androgens. The physiologically active corticoids shown in Figure 15 undergo a multiplicity of further transformations, both in the adrenal itself and in other tissues, notably the liver and sex glands. It is not known at present whether these transformations are related to the hormonal function of these compounds. The catabolic reactions may be classified into four principal groups: oxidative degradation, hydroxylation, reduction and conjugation.

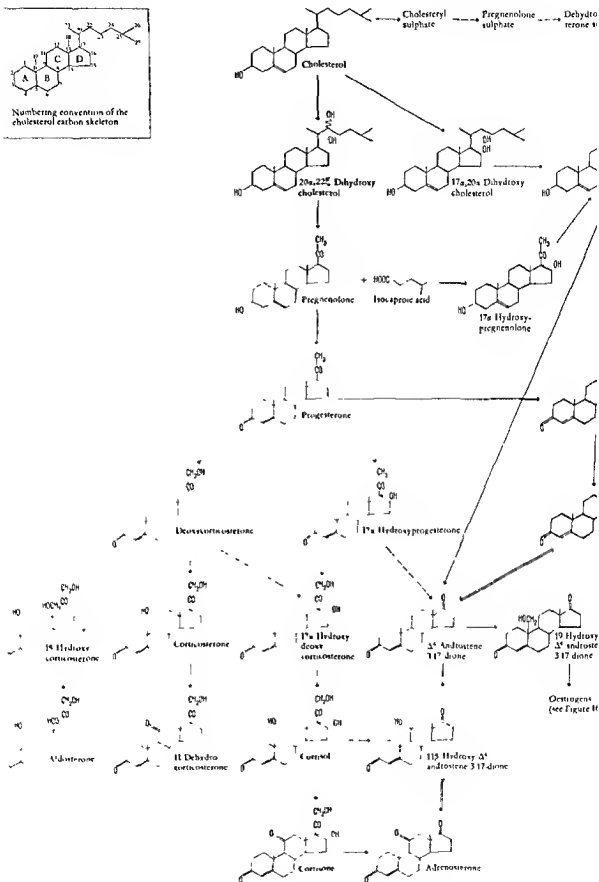
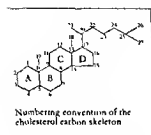
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(continued on p. 429)

Metabolism – Synthesis of Cell Constituents from Glucose

g 15 Biosynthesis of adrenal steroids and androgens



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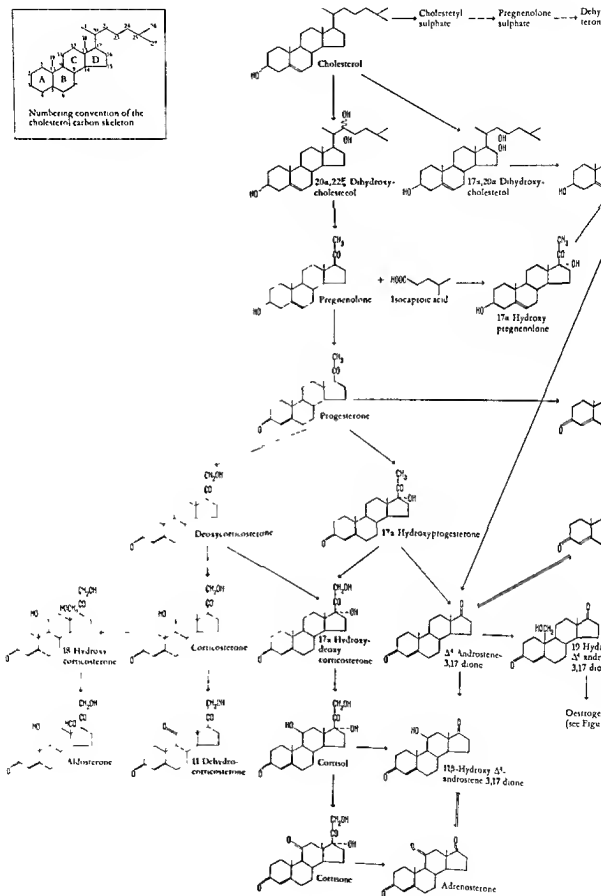
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(continued on page 437)

Metabolism – Synthesis of Cell Constituents from Glucose

Fig 15 Biosynthesis of adrenal steroids and androgens



C₁₁- and C₂₁-) with 16 α -hydroxy groups have also been isolated, and hog adrenal tissue is able to carry out hydroxylations at this position.

Reduction. In general, the body tends to eliminate steroid hormones in the form of metabolites in which the Δ^4 -3-keto system of ring A is totally reduced (Fig. 15). Theoretically, this reduction may lead to products having either 3 α - or 3 β -hydroxy groups and the hydrogen atom at C-5 in either the 5 α - or 5 β -configuration. Actually, almost all reduced metabolites excreted by man are of the 3 α -hydroxy-5 β - (C₁₁: pregnane; C₁₉: aetiocholanone) series. Minor quantities of steroids of the 3 α -hydroxy-5 α - (C₂₁: allopregnane; C₁₉: androstane) series are also excreted. Metabolism of steroid hormones by tissues of other species, in particular rat liver (*in vitro*) yields predominantly (but not exclusively) reduction products of the 5 α -series having both 3 α - and 3 β -hydroxy groups. Reduction of the Δ^4 -3-keto moiety apparently proceeds in stepwise fashion, the Δ^4 -bond being reduced first¹¹. Interesting sex differences have been observed in the intracellular distribution and overall concentration of Δ^4 -steroid reductases in the rat¹².

Conversion of the 20-keto group to a 20-hydroxy group is a further important catabolic reduction of the C₂₁-steroids and also follows a course in most *in vitro* tissue preparations sterically different from that found in man. The product *in vitro* is generally a 20 β -hydroxy derivative; that excreted by man is almost exclusively a 20 α -hydroxy derivative.

Conjugation and excretion. The steroid excretion products of the urine are present largely in the form of conjugates with glucuronic acid or with sulphate. Dehydroepiandrosterone and androstene are present in the urine to a major extent as sulphate conjugates. There is evidence for the secretion of some dehydroepiandrosterone as the sulphate¹³. Some of this material may arise via a series of intermediates derived directly from cholesterol sulphate¹⁴, but the quantitative importance of this pathway remains to be established. Cortisone and cortisol are apparently excreted in the urine largely in the free form, but the majority of the C₂₁-metabolites are excreted as β -glucuronides; the latter appear to arise primarily in the liver by a mechanism involving glucuronosyl transfer from uridine diphosphate glucuronic acid¹⁵. It has been demonstrated that about 50% of the blood cortisol is in the glucuronide form¹⁶.

Pituitary control. The adrenal cortex is maintained in a normal functional state by the action of pituitary ACTH. Apart from this generalized influence on the metabolism of adrenal cortical tissue, ACTH also exerts a specific and immediate stimulating effect on the process of corticosteroid biogenesis. The precise point (or points) at which this influence is exerted is still in doubt. One important point of action is considered to be at a very early stage, probably in the conversion of cholesterol to pregnenolone¹⁷. It has also been observed that ACTH stimulation can alter the ratio of the amounts of cortisol and corticosterone secreted, but such an effect does not necessarily imply intervention of ACTH in the later stages of biosynthesis¹⁸. The mechanism of action of ACTH remains largely unknown at the present time despite intensive study¹⁹. For further discussion of this subject see page 717.

Aldosterone. Aldosterone, the steroid hormone mainly responsible for controlling electrolyte balance, is unique in that it has an aldehydic group at C-18 and is synthesized in the zona glomerulosa of the cortex. Aldosterone production has been demonstrated from a number of precursors but the major route is probably progesterone \rightarrow deoxycorticosterone \rightarrow corticosterone \rightarrow aldosterone (Fig. 15). The major metabolic product seems to be tetrahydroaldosterone glucuronide²⁰. The 18-hydroxytetrahydrocorticosterone found in human urine is a metabolite of 18-hydroxycorticosterone and not of aldosterone²¹.

Since aldosterone output falls by only 30% after hypophysectomy ACTH would appear to have little effect on aldosterone secretion²². More important and more direct is probably the regulation by the sodium and potassium concentrations and the extracellular fluid volume of the body. Angiotensin also plays an important part²³ (see page 741).

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Biosynthesis and metabolism of oestrogens

(For references see page 432)

It is now evident that all the tissues active in the synthesis of steroid hormones are capable of some degree of oestrogen synthesis. Under more usual physiological conditions the ovaries are certainly the most active site of such synthesis, but their output is surpassed several hundred-fold by the placenta close to term.

The oestrogens are C₁₈-steroids in which ring A is aromatic, and there is now ample evidence for the biosynthesis^{1,2} of these compounds from acetate via cholesterol, pregnenolone, progesterone and the C₁₉-steroids, according to the scheme outlined in Figure 16. The aromatization of ring A evidently takes place via a C₁₉-steroid intermediate in which the C-19 methyl group has been oxidized, though whether this intermediate has a hydroxylic or aldehydic oxygen function at C-19 has not been unequivocally established. The C-19 atom is released as formaldehyde³, a finding interpreted as indicating that oxidation at C-19 proceeds to the aldehyde stage prior to rupture of the C-10 to C-19 bond, as shown. Several other mechanisms could, however, yield the same end products. There is evidence that the aromatizing enzyme system has rather low specificity with respect to the structure of the molecule as a whole. Thus, both 6 α - and 6 β -hydroxy- Δ^4 -androstene-3,17-dione are converted to the corresponding 6-hydroxyoestrogens⁴.

Intermediate metabolism of oestrogens

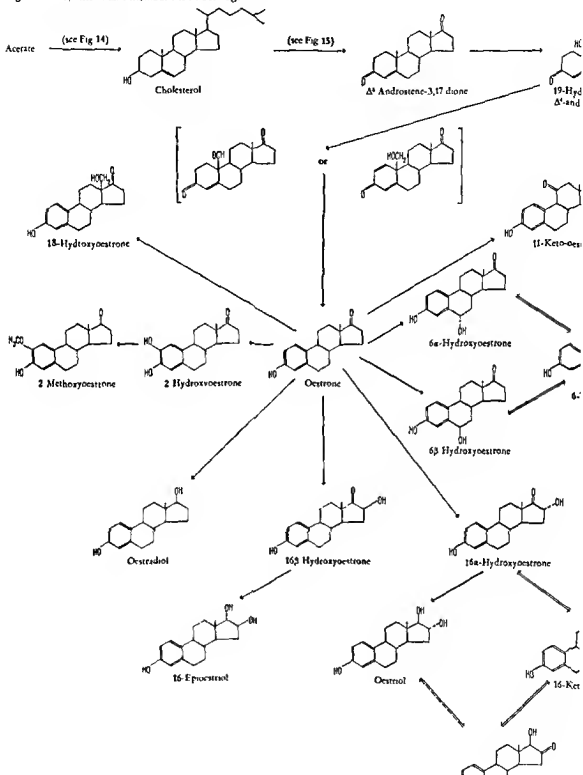
When radioactive oestrone or oestradiol-17 β is administered to intact animals or incubated with animal tissues the oestrogenic activity is rapidly destroyed; considerably less than half of the administered radioactivity can be recovered in the ether-soluble fraction even after hydrolysis of the excreta or the incubation mixture with acid or with enzymes which release the oestrogens from their known conjugated forms^{1,5}. The nature of the oestrogen derivatives that resist extraction with ether in such experiments is entirely unknown, and this fact should not be overlooked when considering the significance of the work relating to oestrogen metabolism summarized in the following sections.

When either oestradiol or oestrone is injected into a human subject, conjugates of the three steroids oestrinol, oestrone and oestradiol-17 β appear in the urine in the approximate proportions 45:45:10. The relative constancy of these proportions indicates a rapid equilibration of oestrone and oestradiol in the body tissues. The enzyme responsible for the interconversion in the human placenta has been studied extensively. It can utilize either NAD or NADP as cofactor, a finding that has prompted speculation as to the mode of physiological action of the oestrogenic hormones⁶.

During the past few years, several other phenolic steroids besides the 'classical' oestrogens - oestradiol, oestrone and oestrinol - have been isolated from various sources and have been characterized chemically. Thus it is now clear that hydroxylation of oestrone may occur at the 2-, 6-, 11-, 16- or 18-position. The interrelationships of these various compounds are shown in Figure 16. Hydroxylation at the 2-position is followed by methylation. Both reactions occur in the liver, and both 2-hydroxy- and 2-methoxyoestrone may be eliminated in the urine. The methylation reaction is catalyzed by an O-methyl transferase which, like other O-methyl trans-

Metabolism – Synthesis of Cell Constituents from Glucose

Fig.16 Biosynthesis and metabolism of oestrogens



16 α -hydroxyoestrone⁹. Very small amounts of 17-epioestril are also formed. 16 β -Hydroxyoestrone is a further product, but on enzymic reduction gives 16-epioestril with 16,17-epioestril as a minor product. 18-Hydroxyoestrone occurs in pregnancy urine¹⁰ and there is evidence that this compound is of adrenal origin¹¹.

Equilin and equilin are well known as urinary oestrogens of the pregnant mare, and equilin has been identified as a metabolite of a feminizing adrenal tumour in man¹². Evidence against the derivation of these compounds from oestrone has been put forward, but since it is based on *in vivo* work with horses it must be accepted with reservation.

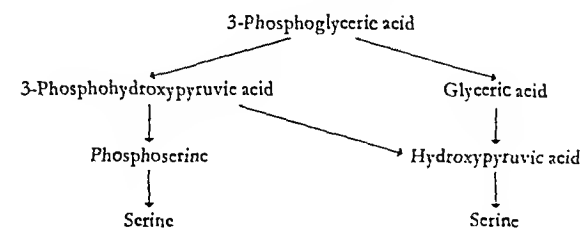
Conjugates of oestrogen metabolites. The urinary oestrogens are excreted predominantly in the form of conjugates with glucuronic acid or sulphate. Oestril is converted to both the 16- and 17-glucuronosides, but the involvement of the phenolic oxygen function in glucuronoside formation has definitely been established in the case of oestrone. This steroid accepts the glucuronic acid residue from UDP-glucuronic acid in a typical reaction catalysed by a glucuronyl transferase¹. The formation of the sulphates involves the phenolic hydroxyl function in the case of oestril and oestrone. The mechanism of this reaction has not been described, but the mechanism of formation of other sulphate esters has been extensively studied¹³.

References

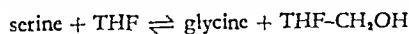
- 1 BREUER, H., *Vitam. and Horm.*, **20**, 285 (1962).
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- 6 TALLALAY and WILLIAMS-ASHMAN, *Proc. nat. Acad. Sci. (Wash.)*, **44**, 15 (1958); TOMKINS and MAXWELL, *Ann. Rev. Biochem.*, **32**, 677 (1963).
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- 9 FISHMAN et al., *J. biol. Chem.*, **235**, 3104 (1960); FISHMAN et al., *Acta endoer. (Kbh.)*, **37**, 57 (1961).
- 10 LOKE et al., *Biochim. biophys. Acta (Amst.)*, **28**, 214 (1958).
- 11 LOKE et al., *Biochim. biophys. Acta (Amst.)*, **26**, 230 (1957).
- 12 SALHANICK and BERLINER, *J. biol. Chem.*, **227**, 583 (1957).
- 13 ROBBINS and LITMANN, *J. biol. Chem.*, **229**, 837 (1957).

Formation of serine and glycine

Serine can be formed from glucose via phosphoglyceric acid. It is not certain at what stage the phosphate is removed from the ester link and the evidence is in accordance with several possibilities¹ as follows:



Glycine is formed from serine by the action of serine hydroxymethyltransferase, the hydroxymethyl group being transferred to tetrahydrofolic acid to form hydroxymethyltetrahydrofolic acid²:

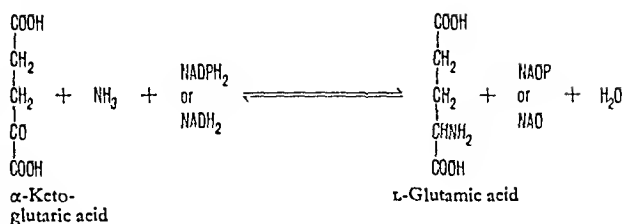


References

- 1 ICHIHARA and GREENBERG, *J. biol. Chem.*, **224**, 331 (1957).
- 2 KISLIUK and SAKAMI, *J. biol. Chem.*, **214**, 47 (1955); ALEXANDER and GREENBERG, *J. biol. Chem.*, **220**, 775 (1956).

Formation of glutamic acid

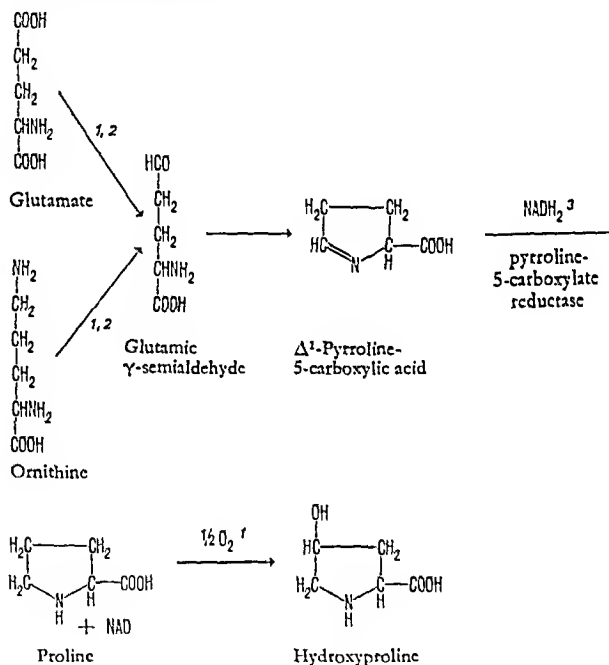
Glutamic acid is readily synthesized in liver and other animal tissues when α -ketoglutarate, ammonia and reduced NAD or NADP are available. The reaction is catalysed by glutamate dehydrogenase:



Glutamic acid is the only amino acid in animal tissues that can be directly synthesized from ammonia and the corresponding carbon skeleton (supplied in the form of the α -ketonic acid). All other nonessential amino acids are formed from the corresponding α -ketonic acids by transamination with glutamate. The reductive amination of α -ketoglutarate is thus the most important ammonia-binding reaction in the animal body.

Formation of proline and hydroxyproline

These amino acids are assumed to be formed from ornithine or glutamic acid via glutamic semialdehyde according to the following sequence of reactions:



Collagen hydroxyproline is derived from proline by hydroxylation of prolyl residues in a precursor polypeptide, the so-called protocollagen³. In an analogous reaction hydroxylysine is derived from peptide-linked lysine⁵.

References

- 1 STETTEN, M.R., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Johns Hopkins Press, Baltimore, 1955, page 277; VOGEL, H.J., *ibid.*, page 335.
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- 4 UOENTRIED, S., *Science*, **152**, 1335 (1966).
- 5 POPENOE et al., *J. biol. Chem.*, **240**, 3089 (1965).

Formation of histidine

The capacity of man to synthesize histidine has not been established. In micro-organisms this amino acid is synthesized from ATP, ribose 5-phosphate 1-pyrophosphate and glutamine in a ten-stage reaction¹.

Reference

- 1 BROQUIST and TRUPIN, *Ann. Rev. Biochem.*, **35**, 231 (1966).

Metabolism - Synthesis of Cell Constituents from Amino Acids

(For references see page 436)

Synthesis of cell constituents from amino acids

include glutamine, glycine, aspartate, etc.

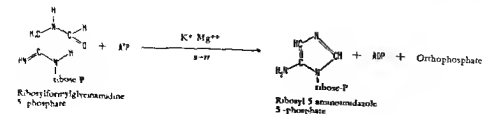
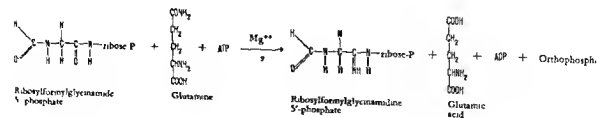
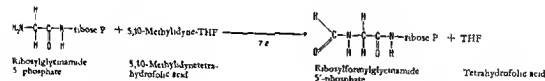
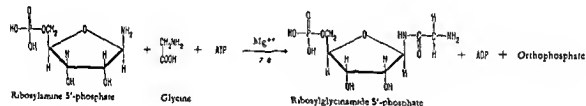
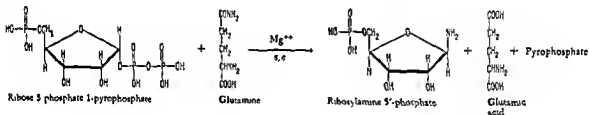
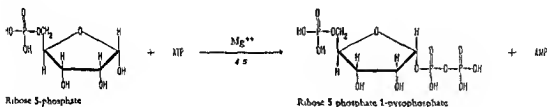
The principal products, their pathways of formation and their biological functions are summarized in Table 20 on page 434

Formation of purines

Knowledge of the pathways shown below and on pages 435 and 36 is derived mainly from work done in 1947

12 amino acid phosphoric acid substrates utilized in this process

Formation of inosinic acid (inosine monophosphate, IMP)



(continued)

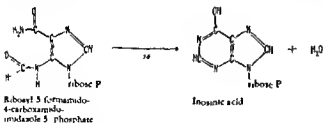
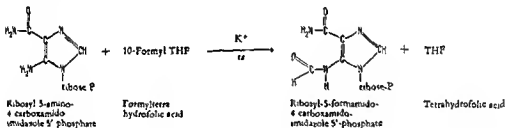
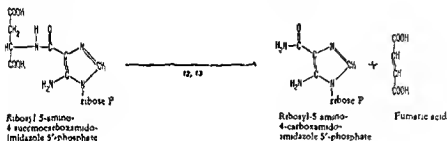
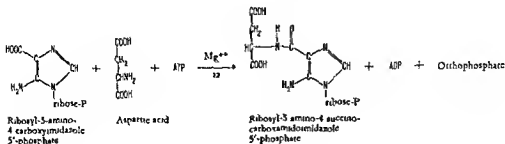
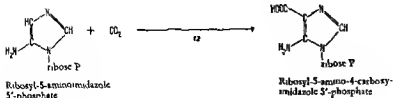
Table 20 Formation of basic cell constituents and metabolites from amino acids

This list is not comprehensive; for carbohydrate synthesis from amino acids see page 441.

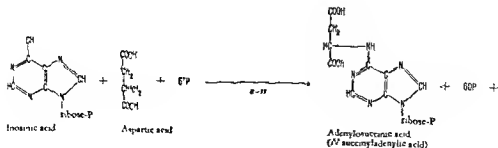
Amino acid serving as starting material	Product formed	Pathway of formation	Physiological function
Glycine	Purine bases	See page 433	Constituent of nucleic acids and nucleotides
	Porphyrins	See page 437	Constituent of haemoglobin and cytochromes
	Creatine	See page 437	Precursor of creatine phosphate, an energy store muscle and other tissues
	Glutathione	See page 438	Coenzyme function in the glyoxalase system and in cis-trans isomerases and probably other enzymes
	Hippuric acid and related compounds	See page 445	Detoxication product of benzoic acid
	Bile acids	See page 438	Required for digestion of fats
Serine	Ethanolamine	Decarboxylation (see Table 6, page 394)	Constituent of phospholipids
	Choline	Methylation of ethanolamine, methionine acting as a methyl group donor	Constituent of phospholipids
	Acetylcholine	Acetylation of choline by acetyl-coenzyme A ¹	Transmitter substance at nerve endings
Cysteine	Taurine	See page 438	Constituent of bile acids
	Glutathione	See page 438	See above under 'Glycine'
Glutamic acid	Glutamine	From glutamic acid and ammonia in the presence of ATP ²	Cell constituent. Intermediate carrier of amino groups in aminations and amidations
	γ -Aminobutyric acid	Decarboxylation (see Table 6, page 394)	Cell constituent, especially of brain
	Glutathione	See page 438	See above under 'Glycine'
	Proline	See page 432	Protein constituent
	Hydroxyproline	See page 432	Protein constituent
Arginine	Creatine	See page 437	See above under 'Glycine'
Methionine	Creatine	See page 437	See above under 'Glycine'
	Choline	Decarboxylation (see Table 6, page 394)	See above under 'Serine'
Histidine	Histamine	Decarboxylation (see Table 6, page 394)	Vasodilator. Stimulates gastric secretion
Aspartic acid	Pyrimidine bases	See page 439	Constituent of nucleic acids and nucleotides
	β -Alanine	Probably by α -decarboxylation	Constituent of special peptides (anserine, carnosine, coenzyme A, pantothenic acid)
Tyrosine	Adrenaline	See page 440	Hormone
	Noradrenaline	See page 440	Hormone and transmitter substance at nerve endings
	Thyroxine	See page 440	Hormone
	Melanins	See page 440	General pigments of hair and skin
Tryptophan	5-Hydroxytryptamine (serotonin)	See page 441	Transmitter substance at nerve endings in the CNS
	Nicotinic acid	See page 399 and 476	Constituent of nicotinamide-adenine dinucleotides
Glucogenic amino acids	Carbohydrates	See page 441	

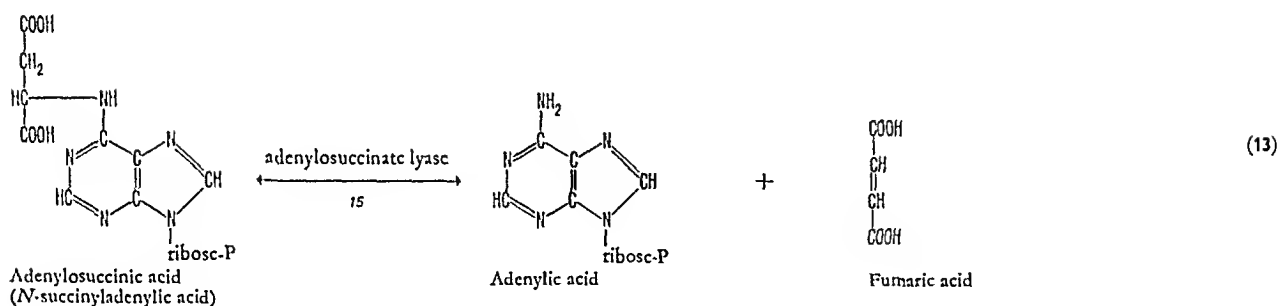
References ¹ KORKES et al., *J. biol. Chem.*, 198, 215 (1952).² ELLIOTT, W.H., *J. biol. Chem.*, 201, 661 (1953).

Metabolism – Synthesis of Cell Constituents from Amino Acids

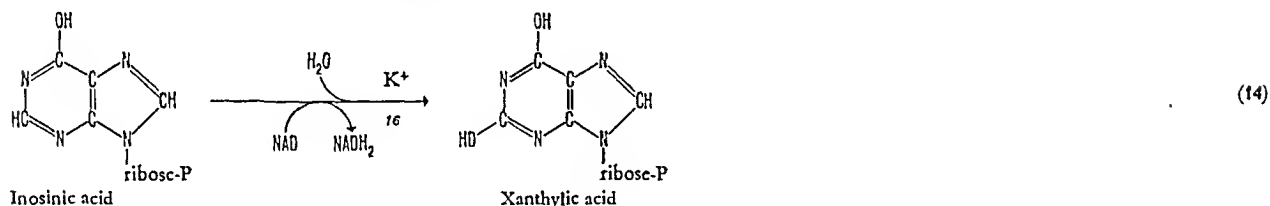


Formation of adenylic acid (adenosine monophosphate, AMP)

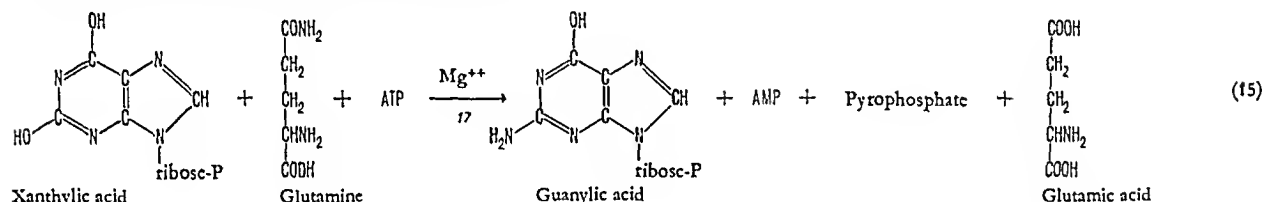




Formation of xanthylic acid (xanthosine monophosphate, XMP)



Formation of guanylic acid (guanosine monophosphate, GMP)

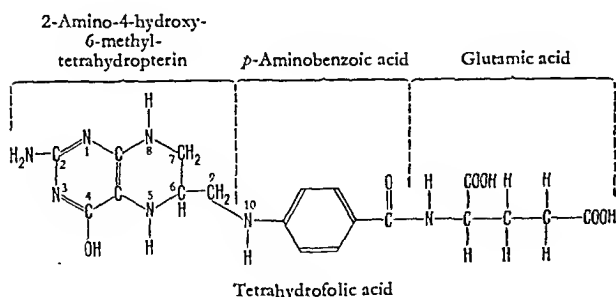


References

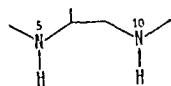
- ¹ CARTER, C.E., *Ann. Rev. Biochem.*, 25, 123 (1956); BUCHANAN and HARTMAN, *Advanc. Enzymol.*, 21, 199 (1959); HARTMAN and BUCHANAN, *Ann. Rev. Biochem.*, 28, 365 (1959).
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- ³ CHRISTMAN, A.A., *Physiol. Rev.*, 32, 303 (1952).
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- ⁶ GOLDTHWAIT, D.A., *J. biol. Chem.*, 222, 1051 (1956).
- ⁷ GOLDTHWAIT et al., *J. biol. Chem.*, 221, 569 (1956); WARREN and BUCHANAN, *J. biol. Chem.*, 229, 613 (1957).
- ⁸ HARTMAN et al., *J. biol. Chem.*, 221, 1057 (1956).
- ⁹ LEVENBERG and BUCHANAN, *J. biol. Chem.*, 224, 1005 and 1019 (1957).
- ¹⁰ MELNICK and BUCHANAN, *J. biol. Chem.*, 225, 157 (1957).
- ¹¹ GOLDTHWAIT et al., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Johns Hopkins Press, Baltimore, 1955, page 765; BUCHANAN et al., in McELROY and GLASS (Eds.), *A Symposium on Amino Acid Metabolism*, Johns Hopkins Press, Baltimore, 1955, page 743.
- ¹² MILLER and BUCHANAN, *J. biol. Chem.*, 237, 485 (1962).
- ¹³ MILLER et al., *J. Amer. chem. Soc.*, 79, 1513 (1957).
- ¹⁴ FLAKS et al., *J. biol. Chem.*, 229, 603 (1957).
- ¹⁵ LIEBERMAN, I., *J. biol. Chem.*, 223, 327 (1956).
- ¹⁶ CARTER and COHEN, *J. biol. Chem.*, 222, 17 (1956).
- ¹⁷ ABRAMS and BENTLEY, *Arch. Biochem.*, 58, 109 (1955); LAGERKVIST, U., *Acta chem. scand.*, 9, 1028 (1955); GEHRING and MAGASANIK, *J. Amer. chem. Soc.*, 77, 4685 (1955).

Transfer of groups containing one carbon atom⁷

Tetrahydrofolic acid (THF) is the coenzyme of many reactions involving the transfer of a group containing one carbon atom. In most cases the one-carbon fragment is attached to nitrogen atoms 5 or 10 of THF, or to both.



For the sake of brevity it is common to draw only the portion of the THF molecule that includes these atoms:

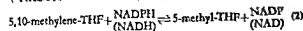
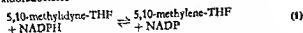


The groups most commonly transferred and their mode of attachment to THF are as follows:

Group attached to one N atom	Group attached to two N atoms	Oxidation state equivalent to
<p>5-Methyl-THF</p>		<p>Methanol</p>
<p>10-Hydroxymethyl-THF</p>	<p>5,10-Methylene-THF</p>	<p>Formaldehyde</p>
<p>5-Formyl-THF (10-formyl-THF also occurs)</p>	<p>5,10-Methyldiene-THF</p>	<p>Formic acid</p>
<p>5-Formimino-THF</p>	<p>5,10-Methyldiene-THF</p>	<p>Formic acid</p>

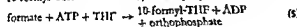
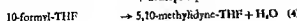
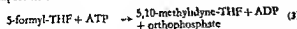
Metabolism - Synthesis of Cell Constituents from Amino Acids

Formyl-THF, hydroxymethyl-THF and methyl-THF are enzymatically interconvertible. The reactions are catalyzed by specific oxidoreductases*

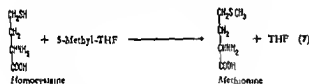


*... .. to 5,10-methylidene-THF by reaction with NADPH, forming a methyl group

importance.



Another important methylation reaction is the formation of methionine from homocysteine (7). Vitamin B₁₂ is involved in this reaction

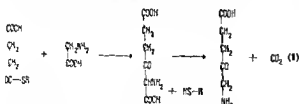


References

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Formation of porphyrins

The synthesis of the porphyrin group of the heme molecule is a complex reaction. The formation of this complex molecule has been demonstrated to proceed via δ -aminolaculnic acid and porphobilinogen² by the following reactions

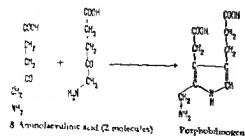


Succinyl-coenzyme A (see page 390)

Glycine

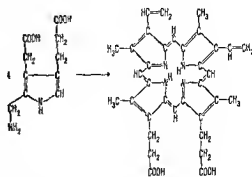
α -Amino- β -ketolaculnic acid (hypothetical intermediate)

δ -Amino laculnic acid



δ -Aminolaculnic acid (2 molecules)

Porphobilinogen



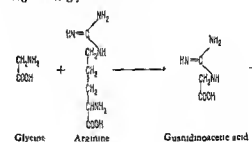
Porphobilinogen

Protoporphyrin IX

References

Formation of creatine from glycine, arginine and

Creatine (which in the form of creatine phosphate store of 'phosphate bond energy' is formed by two reactions. The basic skeleton of creatine is provided by first transfer reaction the group $\text{HN}=\text{C}-\text{NH}_2$ is transferred to glycine

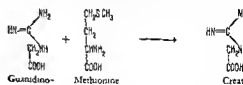


Glycine

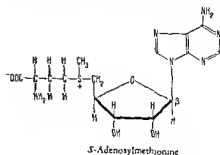
Arginine

Guanidinoacetic acid (glycoylamine)

In the second reaction the methyl group of methionine reacts with the guanidinoacetic acid formed in the first

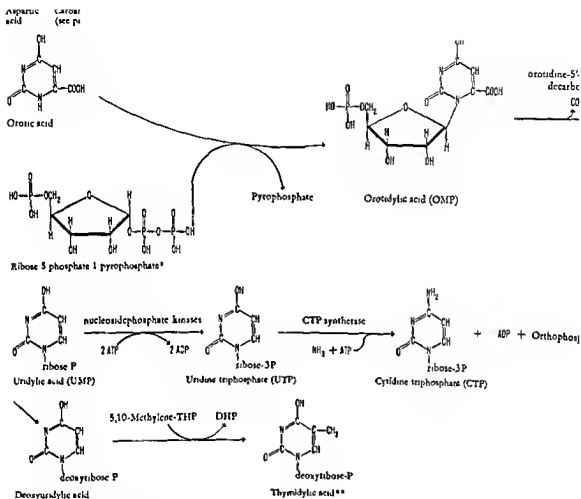


Methionine does not react as the free amino acid; it reacts as an adenosyl derivative, formed from ATP and methionine



S-Adenosylmethionine

Homocysteine appears likewise as the adenosyl derivative in the transmethylation reaction formulated above.³ Creatine interacts reversibly with ATP, especially in the form of creatine phosphate.



¹ This compound is formed by reaction (1), page 433

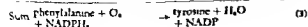
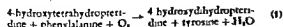
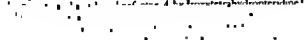
** Strictly speaking, this compound should be termed deoxythymidylic acid (dTMP) since it contains deoxyribose

References

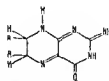
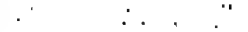
¹ CASPER, C.E., *Acc. Res. Biochem.*, 25, 123 (1956) LOWENSTEIN and COHEN, *J. Biol. Chem.*, 220, 57 (1956), COOPER et al., *J. Biol. Chem.*, 216, 37 (1955)

Conversion of phenylalanine to tyrosine

The enzymic conversion of phenylalanine to tyrosine involves a pyridine cofactor. The reaction can be considered to proceed in two parts. The first consists of a hydroxylation involving molecular



A typical form of 4-hydroxydihydropteridine

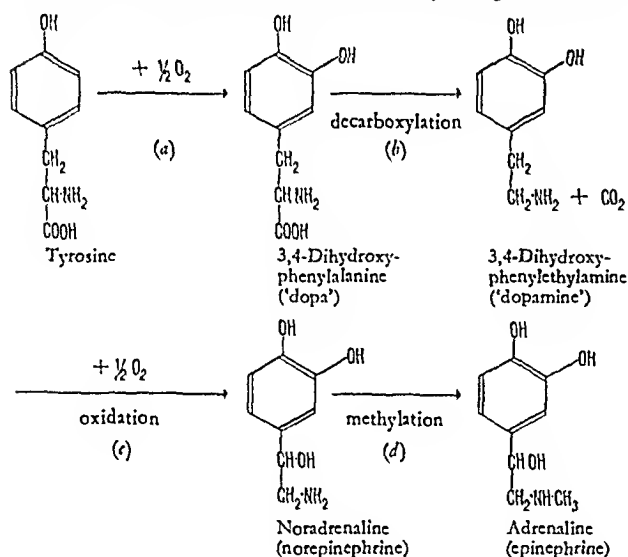


Reference

* KAWAMURA, S., *J. Biol. Chem.*, 239, 332 (1964)

Formation of noradrenaline and adrenaline from tyrosine

Noradrenaline and adrenaline are formed from tyrosine (and thus from phenylalanine), the main pathway being as follows¹:



Enzymes

- (a) tyrosine hydroxylase
 (b) dopa decarboxylase
 (c) dopamine hydroxylase
 (d) phenylethanolamine *N*-methyltransferase

The reaction catalysed by tyrosine hydroxylase is probably the rate-limiting step². The enzyme phenylethanolamine *N*-methyltransferase is found almost exclusively in the adrenal gland³.

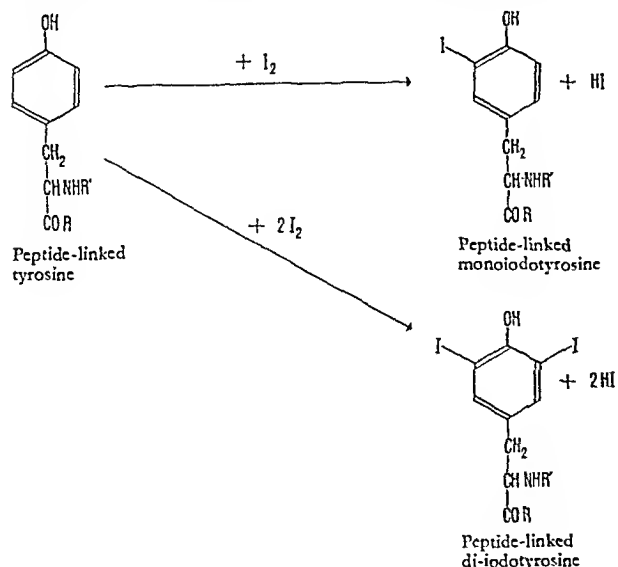
Alternative pathways have been proposed⁴.

References

- ¹ For a review see BLASCHKO, H., *Pharmacol. Rev.*, **11**, 307 (1959).
² LEVITT et al., *Pharmacol. exp. Ther.*, **198**, 1 (1965).
³ AXELROD, J., *J. Biol. Chem.*, **237**, 1657 (1962).
⁴ AXELROD, J., *Science*, **190**, 499 (1963); KOPIN, I. J., *Z. klin. Chem.*, **2**, 115 (1964); IVERSEN, L. L., *Nature*, **219**, 8 (1967).

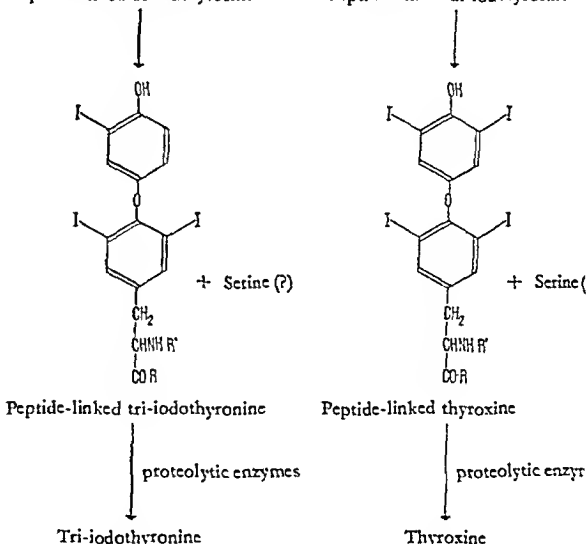
Formation of thyroid hormones¹

Iodide is absorbed in the gastrointestinal tract and rapidly distributed in the extracellular fluid. Except during the postprandial period the iodide concentration of plasma is less than 5 µg/l. This inorganic iodide of the plasma is removed almost entirely by the kidneys and thyroid gland. The concentration of readily exchangeable iodine in the normal thyroid in terms of whole tissue or of tissue water may be 20-40 or more times greater than that in the plasma. Prior to the iodination of the tyrosine molecule the iodide



Peptide-linked monoiodotyrosine
+
Peptide-linked diiodotyrosine

Peptide-linked diiodotyrosine
+
Peptide-linked diiodotyrosine



must be oxidized to free iodine or the iodonium ion, a reaction probably involving a peroxidase. The iodination of tyrosine monoiodotyrosine and diiodotyrosine probably takes place peptide-linked tyrosyl residues. The thyroid hormones triiodothyronine and thyroxine are formed by condensation of iodotyrosyl residues, the side chain of one tyrosyl residue giving rise to serine in this coupling reaction.

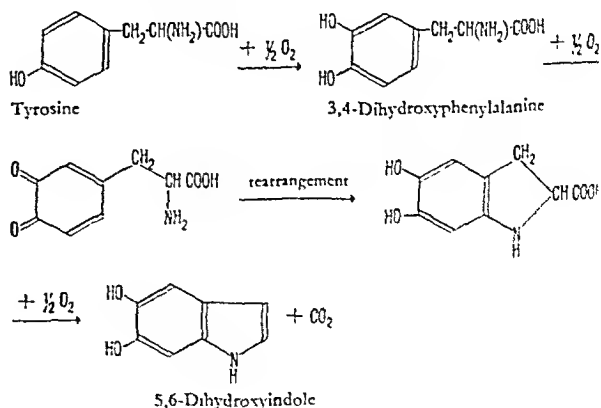
Triiodothyronine and thyroxine are retained in the thyroid within the colloid as peptide-linked residues in the specific protein thyroglobulin. The thyroid hormones are released from the thyroglobulin pool by enzymatic hydrolysis as required. The further metabolism of these hormones is described on pages 726-72

References

- ¹ For a review see ROCHE and MICHEL, *Physiol. Rev.*, **35**, 583 (1955); ROCHER et al., in FLORKIN and MASON (Eds.), *Comparative Biochemistry*, vol. 5, Academic Press, New York, 1963, page 514; STANBURY, J. B., in STANBURY et al. (Eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966, page 215.

Formation of melanin from tyrosine¹

Melanin is the pigment of vertebrate skin, hair, feathers and eye (see page 722). It is a complex and nonhomogeneous substance. The chief basic unit is 5,6-dihydroxyindole, which undergoes polymerization and in the polymerized form combines with protein². It is formed from tyrosine, probably by the following route (this route is blocked in albinism; cf. page 448):



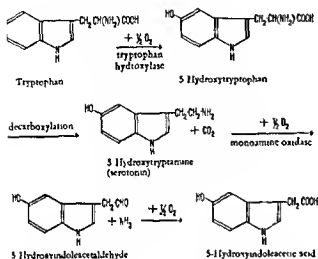
References

- ¹ For a review see MASON, H. S., *Advanc. Enzymol.*, **16**, 163 (1955); DALGLISH, C. E., *Advanc. Protein Chem.*, **10**, 65 (1955).
² CROMARTIE and HARLEY-MASON, *Biochem. J.*, **66**, 713 (1957).

Metabolism – Synthesis of Cell Constituents from Amino Acids

formation and degradation of 5-hydroxytryptamine (serotonin)

5-Hydroxytryptamine (serotonin) is assumed to be a neurotransmitter substance in the CNS, it may play a role in haemostasis, in



The reaction catalysed by the enzyme tryptophan hydroxylase is probably the rate-limiting step in the synthesis of serotonin¹. Serotonin is the precursor of melatonin in the pineal gland (see page 730).

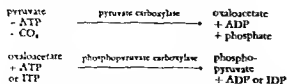
References

- ¹ ESPARtero, V., *Pharmacol. Rev.*, **6**, 425 (1954). SECTON and WILKINSON, *Nature*, **179**, 318 (1957). PAGE, I.H., *Physiol. Rev.*, **38**, 277 (1958).
- ² PAGE, I.H., *Lancet*, **1**, 198 (1955). FARNOW and WALDENSTROM, *Lancet*, **2**, 951 (1954).
- ³ JACOBSON et al., *Molec. Pharmacol.*, **3**, 274 (1967).

Synthesis of carbohydrate from amino acids and other non-carbohydrate precursors (gluconeogenesis)

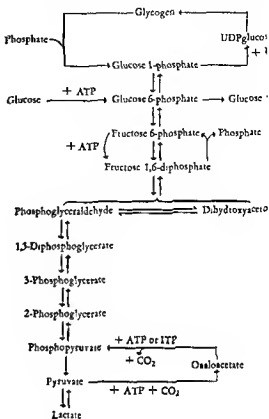
ability to yield pyruvate (or phosphopyruvate). The pathway from pyruvate to glucose includes most steps of the anaerobic glycolysis (Table 3, page 387) in reverse, but at three stages special reactions occur¹ circumventing the energy barriers which would prevent a simple reversal of glycolysis.

(a) The formation of phosphopyruvate from pyruvate. The special reactions by which phosphopyruvate is formed are²

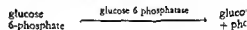


(b) Fructose 1,6-diphosphate is converted into fructose 6-phosphate by a specific phosphatase³ (and not by transfer of phosphate to ADP)

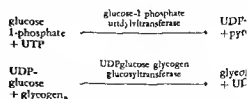
Fig 17 Pathways of carbohydrate breakdown and synthesis. The pathways differ at four points. Breakdown reactions indicated by the left hand arrows, synthesis reactions indicated by the right hand arrows.



(c) Glucose 6-phosphate is likewise dephosphorylated to glucose⁴ (and not by transfer to ADP)



(d) Glucose 1-phosphate is converted into glycogen⁵ and not by reversal of the phosphorylase



The stages of carbohydrate synthesis from pyruvate are indicated in Figure 17 above

References

- ¹ WILKINSON, I.H., *Nature*, **179**, 318 (1957).

Detoxication mechanisms

A number of metabolic processes do not fall under the headings of either energy supply or synthesis of cell constituents. Their common feature is the disposal of potentially harmful substances. In other words they contribute towards the maintenance of the physiological environment. These metabolic processes are commonly referred to as 'detoxication mechanisms'.

Quantitatively the most important detoxication mechanism is the conversion of surplus nitrogen, in particular surplus ammonium ions, into urea (see below). Other detoxication reactions concern the disposal of certain ingested materials (e.g., benzoic acid) and of drugs. A recent review of drug metabolism can be found in GOLDSTEIN *et al.*¹

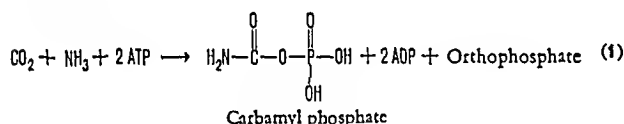
Reference

¹ GOLDSTEIN *et al.*, *Principles of Drug Action*, Harper & Row, New York, 1968.

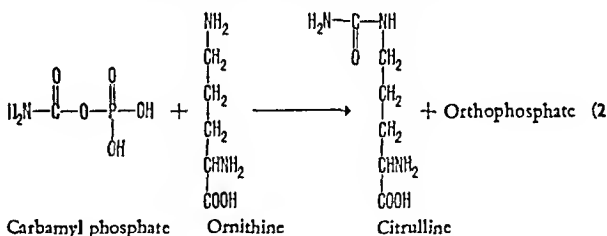
Synthesis of urea¹ (for references see page 444)

Most of the surplus nitrogen arising in the mammalian body is excreted in the form of urea. The synthesis of urea from ammonia and carbon dioxide proceeds by a cyclical mechanism. The concept of the urea (or ornithine) cycle was originally based on the observation that ornithine, citrulline and arginine stimulate urea production in the presence of ammonia without being themselves consumed in the process². Since it was proposed, this concept has received support from many other experiments¹. The reactions of the cycle involve the stepwise building-up of the urea structure on the δ -amino group of ornithine. The building-up process is completed with the formation of arginine, which is then hydrolysed by arginase to yield urea and ornithine.

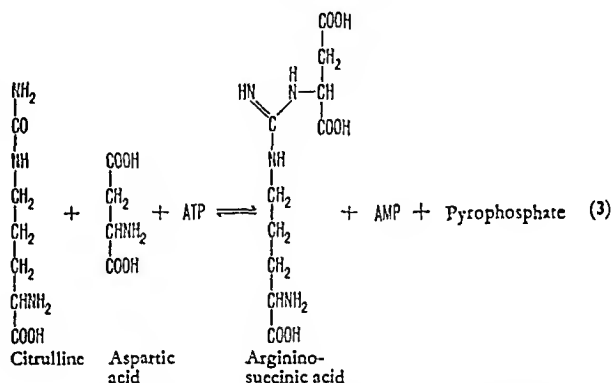
Before one molecule each of ammonia and carbon dioxide enter the cycle, they react to form carbamyl phosphate. The synthesis of this compound requires ATP and has been formulated as follows^{3, 4}:



Reaction (1) is stimulated by acetylglutamate and by other acylglutamates⁵. It is probable that acetylglutamate is the compound normally involved since it occurs in mammalian liver⁶. In bacteria the stimulation by acetylglutamate does not occur, and only one molecule of ATP is utilized per molecule of carbamyl phosphate formed. The nature of the action of acetylglutamate is obscure. Carbamyl phosphate reacts with ornithine to yield citrulline^{2, 7}

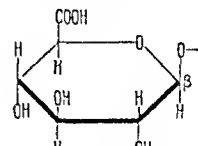


Citrulline next condenses with aspartic acid to form arginino-succinic acid⁸, a process that requires ATP:

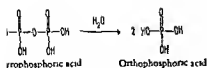


Reaction (3) is freely reversible, but under physiological conditions it proceeds only from left to right because of the presence of a highly active pyrophosphatase⁹:

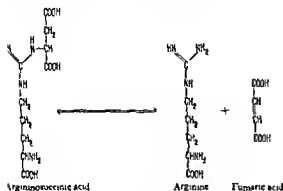
Table 21 Detoxication mechanisms

Reaction	Examples of compounds detoxicated	Product formed	Mechanism
Acetylation	Sulphanilamide	Acetylsulphanilamide	See page 444
Methylation	Nicotinamide	N-Methylnicotinamide	The methyl group is derived from methionine probably via S-adenosylmethionine (see page 437)
Glycine conjugation	Benzoic acid	Hippuric acid	See page 444
Alkyl- and arylglucuronide formation	Alcohols and phenols (menthol and phenol)	Menthyl- and phenylglucuronide	$\text{R} \cdot \text{OH} + \text{UDPglucuronic acid} \rightarrow$  $+ \text{UDP}$ β -Glucuronide
Acylglucuronide formation	Aromatic acids (benzoic acid) and branched-chain aliphatic acids	Benzoylglucuronide	Not known
Sulphate ester formation	Phenols	Phenyl sulphate	See page 445
Glutamine conjugation	Phenylacetic acid	Phenacetylglutamine	See page 445
Mercapturic acid formation	Naphthalene, alkyl halides	Naphthylmercapturic acid	See page 445

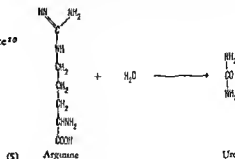
Metabolism – Detoxication Mechanisms



Argininosuccinate reacts further to give arginine and fumarate¹⁰ by reaction (5):



(4) This is followed by the hydrolysis of arginine urea. Ornithine can then undergo the same as starting with reaction (2):



The earlier sequence of the reactions is as follows:



Fig 18 The urea cycle (ornithine cycle)

A list of the enzymes involved in the cycle is given below the diagram

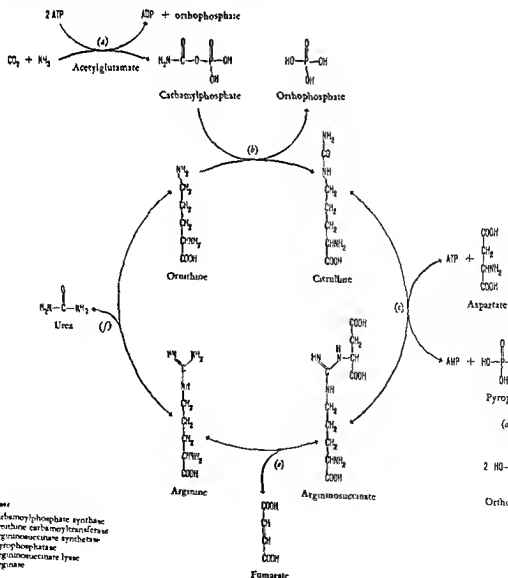
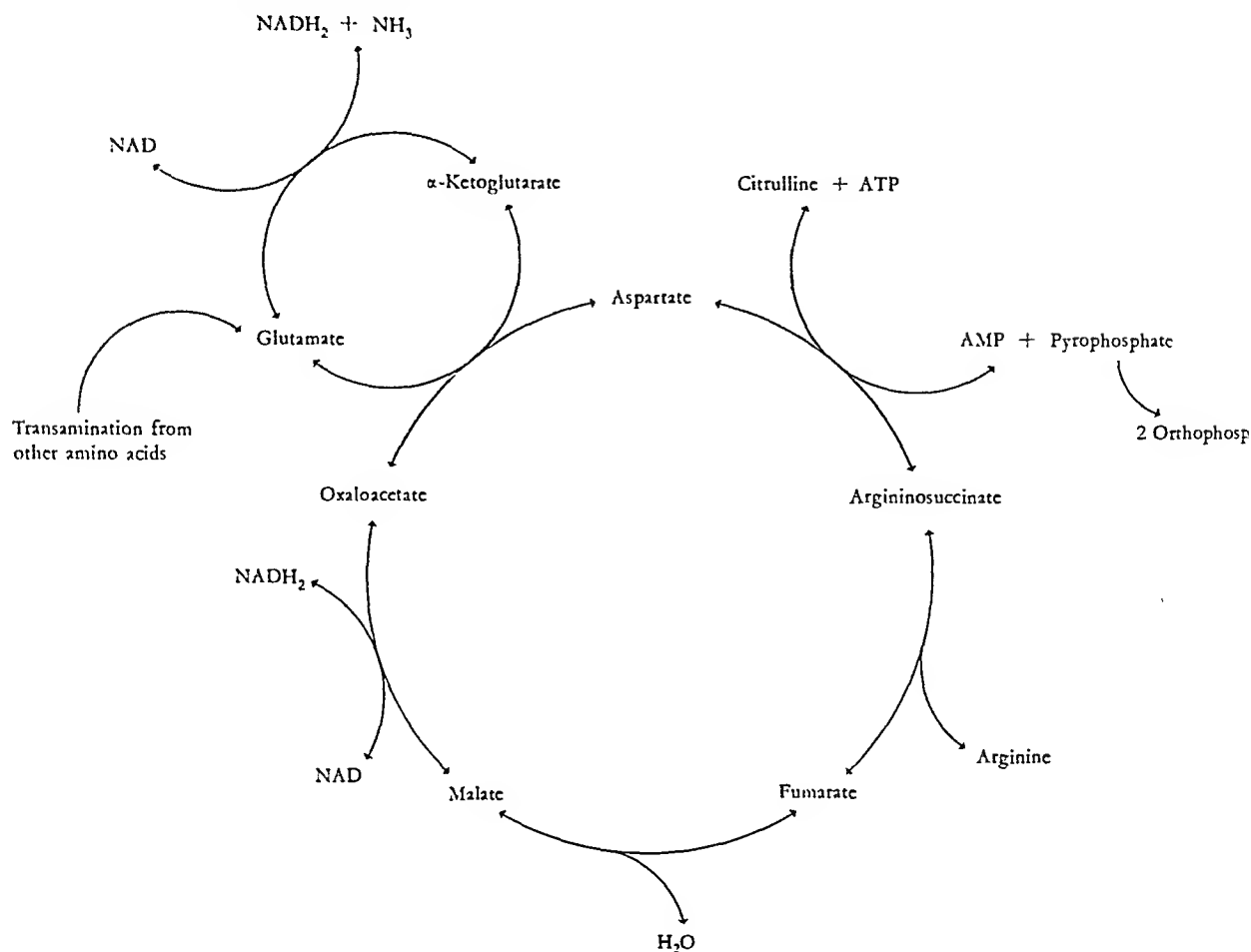
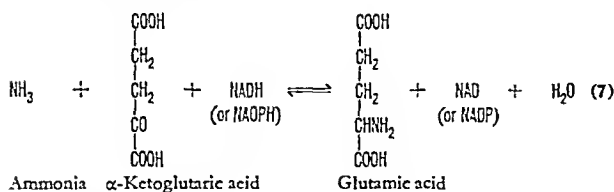


Fig. 19 Utilization and regeneration of aspartate in the synthesis of urea



and α -ketoglutarate (see page 393) or by reductive amination from ammonia and α -ketoglutarate¹¹:



The second nitrogen atom of urea must thus pass through glutamate and aspartate but not necessarily through the stage of ammonia. The supply of aspartate for reaction (3) involves two cycles, which are subsidiary to the main urea cycle shown in Figure 18. These subsidiary processes are shown in Figure 19, above.

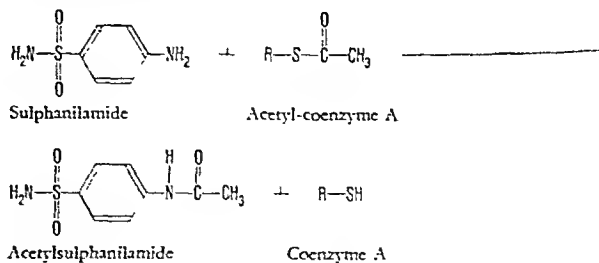
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Acetylation of amines¹

Many aromatic and aliphatic amines are acetylated in the body. These include sulphanilamide, *p*-aminobenzoic acid, *p*-nitraniline and others². In general, the acetylated amines are less toxic than the unacetylated compounds. However, in some cases the low solubility of acetylated amines can render them harmful owing to their crystallization in the urinary tract.

The acetylation reaction proceeds via acetyl-coenzyme A (see page 391), for example:



References

- TAROR et al., *J. biol. Chem.*, 204, 127 (1953); LIPMANN, F., *Bact. Rev.*, 17, 1 (1953).
- WILLIAMS, R.T., *Detoxication Mechanisms*, 2nd ed., Chapman & Hall, London, 1959; WILLIAMS, R.T., *Chm. Pharmacol. Ther.*, 4, 234 (1963).

Formation of glycine conjugates

Aromatic acids such as benzoic acid, nicotinic acid, cinnamic acid and similar compounds are conjugated with glycine in various organs¹. The reaction requires coenzyme A and ATP, and pro-

Introduction

A number of diseases are now known to be caused by a failure of the body to synthesize sufficient quantities of one specific protein, often an enzyme, or by the synthesis of an abnormal protein in place of the normal one. Failure to synthesize an enzyme can cause a complete or partial block of a metabolic pathway and usually leads to the accumulation of the intermediary metabolite that is normally the substrate of the missing enzyme. In some cases the accumulation of this metabolite leads to abnormal side reactions. In phenylketonuria, for example, absence of phenylalanine 4-hydroxylase leads to accumulation of phenylalanine, some of which is converted to phenylpyruvic acid, and this undergoes further changes to *o*-hydroxyphenylacetic acid, phenyl-lactic acid and phenylacetylglutamine.

In some cases the defective protein is not an enzyme in the narrower sense, i.e., a catalyst bringing about a chemical change, but a substance concerned with the active transport of a metabolite from one compartment of the body to another. Examples are intestinal absorption and renal tubular reabsorption. In such cases the resulting disease or abnormality is not caused by a metabolic block but by a disturbance of transportation and the secondary effects of this disturbance. In Hartnup disease, for example, tryptophan is poorly absorbed from the intestine and in consequence

acted on by bacteria in the colon to produce abnormal into compounds that are absorbed. In this disease there is also a renal tubular defect leading to amino-aciduria.

These defects in the synthesis of an enzyme or transport mechanism are genetically determined and are referred to as inborn errors of metabolism. Some defects of this kind consisting of single enzyme failures can be acquired, like the action of a heavy metal poison on proximal renal tubular transport of amino acids and hexachlorobenzene on porphyrin metabolism or the production of alkaptonuria in experimental animals by administration of α , β -dipyridyl. Such acquired defects are often temporary.

Some gene mutations lead to the formation of an abnormal structural protein rather than the absence of an enzyme. The clearest examples are the haemoglobinopathies, where the structure of some of the abnormal proteins has been completely elucidated. In the thalassaemias there is a relative failure to synthesize haemoglobin rather than production of an abnormal haemoglobin. Thalassaemia is thought to be caused by mutation of a 'controller' or 'tap' gene, abnormal haemoglobins by mutations of 'structural' genes. Inborn errors of metabolism may resemble either type of haemoglobinopathy: mutation of the relevant structural gene would produce in place of the normal enzyme a protein lacking catalytic properties, while a 'silent gene' mutation would produce neither the enzyme nor an abnormal protein.

Haemoglobinopathies¹

Four major types of haemoglobin occur in normal erythrocytes: Hb-A₁ (or A), Hb-A₂, Hb-F and Hb-A₃. In the adult, Hb-A₁ constitutes over 85% of the normal haemoglobin and Hb-A₂ about 2½%. Hb-F is the major constituent in utero but is rarely detectable after the first year of extrauterine life. Hb-A₃ is a compound of Hb-A₁ and glutathione found in older erythrocytes and will not be further considered.

Each molecule of haemoglobin consists of four polypeptide chains of two different types and four haem groups. Hb-A₁ has two α^A and two β^A polypeptide chains; Hb-A₂ can be formulated as $\alpha_2^A\beta_2^A$, Hb-A₃ as $\alpha_2^A\delta_2^A$ and Hb-F as $\alpha_2^F\gamma_2^F$. The synthesis of each type of polypeptide chain, α , β , γ or δ , is controlled by a different pair of genes. Each polypeptide consists of between 140 and 150 amino-acid residues. The identity of the amino-acid residue at any point on the chain is determined by the structure of the triplet of deoxyribonucleotides at the corresponding point on the DNA chain constituting the gene. A change in this triplet (i.e., a mutation) may alter the identity of the amino acid incorporated at this point in the chain and thus produce a different polypeptide. Combination of this abnormal polypeptide with other polypeptide chains and haem groups produces an abnormal haemoglobin.

Over 100 different abnormal haemoglobins are known, each produced by a mutation affecting one type of polypeptide chain. In sickle-cell anaemia, for example, the β gene has undergone mutation to produce an abnormal β polypeptide (β^S) with valine in place of glutamic acid at position 6, but the α gene is normal. The major haemoglobin produced by the homozygote is therefore $\alpha_2^A\beta_2^S$, accompanied by normal $\alpha_2^A\gamma_2^F$ and $\alpha_2^A\delta_2^A$; the heterozygote has $\alpha_2^A\beta_2^A$ as well.

Hydrolysis of haemoglobin or its separated polypeptides with trypsin breaks up the chains wherever a lysine or arginine residue occurs, producing a series of oligopeptides. These can be separated by paper electrophoresis and chromatography to produce a two-dimensional pattern of peptides characteristic of the starting protein, a so-called 'fingerprint'. In an abnormal haemoglobin one tryptic peptide in general will differ from its normal counterpart in one of the constituent amino acids and hence in its position (and possibly reactions) on the 'fingerprint'. The relevant peptide spot can be cut out and further analysed.

An abnormal haemoglobin is first denoted by a letter or geographical location or by both, for example Hb-S, Hb-Norfolk, Hb-D_{Punjab}. When it is known which polypeptide chain is abnormal the nomenclature is modified, for example Hb-S = $\alpha_2^A\beta_2^S$, Hb-Norfolk = $\alpha_2^{\text{Norfolk}}\beta_2^A$. The tryptic peptides of the α chain are numbered αTpI to αTpXIV , those of the β chain βTpI to βTpXV ; if known, the tryptic peptide containing the changed amino-acid residue is indicated, for example Hb-S = $\alpha_2^A\beta_2^S = \alpha_2^A\beta_2^{\text{TpI}}$.

Hb-Norfolk = $\alpha_2^{\text{Norfolk}}\beta_2^A = \alpha_2^{\text{TpVII}}\beta_2^A$. The alteration in amino-acid composition, when known, is indicated by, for example, Hb-S = $\alpha_2^A\beta_2^{\text{TpI(Glu} \rightarrow \text{Val)}}$, Hb-Norfolk = $\alpha_2^{\text{TpVII(Gly} \rightarrow \text{Asp)}}$. Finally, when the structure is completely elucidated, the notation used gives the amino acid substituted for the normal one in Hb-A and the position in the polypeptide at which the substitution occurs, for example, Hb-S = $\alpha_2^A\beta_2^{\text{Val}}$, Hb-Norfolk = $\alpha_2^{\text{Asp}}\beta_2^A$. A similar notation applies to the γ and δ chains, though as yet few abnormalities of these have been described.

The thalassaemias are a group of genetically determined anaemias in which the production of α chains, β chains or β + δ chains is greatly decreased or absent. Each type of thalassaemia is carried by a single autosomal gene with heterozygote expression and more marked homozygote expression.

Where α , β or δ chains are produced they are normal in structure; the various thalassaemias are probably caused by mutations of 'tap' genes controlling the activity of the α , β or β + δ structural genes respectively. If α chains are not made, Hb-A₁, Hb-A₂ and Hb-F cannot be formed. Homozygotes for α -thalassaemia probably all die in utero, while heterozygotes have more or less severe anaemia. Since surplus β , γ and δ chains are produced, α -thalassaemias sometimes possess abnormal haemoglobins with four β chains (Hb-H), four γ chains (Hb-Bart's) and, probably, four δ chains. In β -thalassaemia no abnormal haemoglobins are present but Hb-A₁ is decreased in amount or completely absent. In a pure β -thalassaemia, Hb-A₂ is increased in amount, as is Hb-F, but in thalassaemias where the activity of both β and δ genes is reduced, Hb-A₂ as well as Hb-A₁ is decreased in amount. Except in the High Hb-F condition, all homozygotes for β -thalassaemia and 95% of heterozygotes for α - or β -thalassaemia exhibit morphological abnormalities of the erythrocytes in the form of hypochromia, poikilocytosis, frequent target cells and microcythemia. The erythrocytes show decreased osmotic fragility. The anaemia is caused both by reduced formation of the globin moiety of haemoglobin and by haemolysis.

Thalassaemias are classified on clinical grounds. Probably all homozygotes for β -thalassaemia have thalassaemia 'major', and the majority of heterozygotes thalassaemia 'minor', 'minima' or 'trait'. There is some overlapping, however, as with heterozygotes for α -thalassaemia, who may show any degree of anaemia from very mild to very severe.

The High Hb-F gene is classified with the thalassaemias since it suppresses formation of β and δ chains. However, it is clinically harmless even when combined with sickle-cell trait in double heterozygotes. The High Hb-F condition has been called 'nonmicrocytic haemic thalassaemia'².

Hb-Lepore and related diseases in homozygous form closely resemble the β -thalassaemias clinically as well as in the morphology of the erythrocytes and in the high proportion of Hb-F in the blood. In the Hb-Lepore group, however, an abnormal haemoglobin is present in place of Hb-A₁ and Hb-A₂. This abnormal haemoglobin has normal α chains but in place of β or δ chains a hybrid of these two. These abnormal β/δ polypeptides are formed

* This chapter on 'Inborn Errors of Metabolism' has been written in collaboration with L.I. WOLFE (Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford).

probably by nonhomologous crossings over of the β and δ genes, which are adjacent².

Although most abnormal haemoglobins are found only very rarely, the genes for thalassaemia (Hb-S, Hb-C and Hb-E) occur with high frequency in some parts of the world. Some of these,

be found for the markedly uneven geographical distribution of the genes for Hb-C and Hb-E.

Some representative haemoglobinopathies are listed in Table 1

References

Table 1 Haemoglobinopathies and thalassaemias

Condition or abnormal haemoglobin	Haemoglobins present	Clinical features	Original geographical distribution
Sickle-cell anaemia	$\alpha_1^A\beta_1^S$ (Hb-S) 77-87% $\alpha_1^A\beta_1^S$ (Hb-A ₂) 2.5% $\alpha_1^A\gamma_1^F$ (Hb-F) 10-20%	Infarcts and haemolytic anaemia	Central and West Africa, India, South Arabia, Mediterranean lands
Sickle-cell trait (heterozygotes for above)	$\alpha_1^A\beta_1^A$ (Hb-A ₁) 56-76% $\alpha_1^A\beta_1^S$ (Hb-S) 20-40%	Usually symptomless, sickling crises if anoxic	As above
Hb-C disease	$\alpha_1^A\beta_1^{Cys}$ 88% $\alpha_1^A\beta_1^A$ 9% $\alpha_1^A\gamma_1^F$ 2%	Fairly mild haemolytic anaemia, splenomegaly	Northern Ghana
Hb-SC disease (heterozygote for Hb-S and Hb-C)	$\alpha_1^A\beta_1^S$ 52.5% $\alpha_1^A\beta_1^{Cys}$ 43.5% $\alpha_1^A\gamma_1^F$ 3.5%	Severe haemolytic anaemia	Parts of Ghana and neighbouring countries
Hb-E	$\alpha_1^A\beta_1^{Eys}$	Relatively mild anaemia	Thailand, South-east Asia
Hb-G ₁₀₀₂₀₀₀	$\alpha_1^A\beta_1^{G1002000}$	Symptomless	-
Hb-AI group (at least 3 different types)	Hb-M _{Boston} = $\alpha_1^A\gamma_1^{V12U111+222}$ β_2^A	Methaemoglobinemia, fairly severe anaemia	Europe (?)
Hb-Zürich	$\alpha_1^A\beta_1^{Zürich}$	Sulphonamides produce haemolytic crises	Europe (?)
Hb-Lepore (at least 3 forms: Hb-Lepore _{San Jose} , Hb-Lepore _{Malabar} , Hb-Pylos)	Hb-Lepore 25% $\alpha_1^A\gamma_1^F$ 75%	As in β -thalassaemia	-
δ Thalassaemia	$\alpha_1^A\delta_1^A$ reduced (none in homozygotes)	None, unless combined with β - or ($\delta\beta$)-thalassaemia	Greece
($\delta\beta$)-Thalassaemia (1 thalassaemia)	$\alpha_1^A\delta_1^A$ none or reduced $\alpha_1^A\delta_1^A$ up to 100% in homozygotes $\alpha_1^A\gamma_1^F$ 5-15% in heterozygotes	As for β thalassaemia	Greece, Central Africa

Table 1 (continued) Haemoglobinopathies and thalassaemias

Condition or abnormal haemoglobin	Haemoglobins present		Clinical features	Original geographical distribution
β -Chain thalassaemia (COOLEY's anaemia, Mediterranean anaemia, thalassaemia major, A_2 -thalassaemia, etc.)	$\alpha_1^A\beta_1^A$ $\alpha_1^A\gamma_1^F$ $\alpha_1^A\delta_1^A$	none or low 5-95% 2-14%	Severe microcytic anaemia	Mediterranean lands, Asia south of latitude 40°N, Central Africa
High Hb-F (persistent foetal haemoglobin, F-gene, 'non-microcythaemic thalassaemia')	$\alpha_1^A\gamma_1^F$	100% in homozygotes 30% in heterozygotes	Symptomless; total Hb concentration normal even in homozygotes	Central Africa (?)
Heterozygotes for β -chain thalassaemia (COOLEY's trait, thalassaemia minor)	$\alpha_1^A\beta_1^A$ $\alpha_1^A\delta_1^A$ $\alpha_1^A\gamma_1^F$	reduced raised in 96% raised in 50%	Microcytic anaemia, varying from very mild to severe	Mediterranean lands, etc.
Heterozygotes for β -chain thalassaemia and Hb-S, Hb-C or Hb-E (sickle-cell thalassaemia, etc.)	$\alpha_1^A\beta_1^S$ Val or $\alpha_1^A\beta_1^C$ Lys or $\alpha_1^A\beta_1^E$ Lys		Combine the features of both heterozygous diseases; often more severe than either alone	As for Hb-S, Hb-C or Hb-E
α -Chain thalassaemias, Hb-H, Hb-Bart's (COOLEY's anaemia, etc.)	$\alpha_1^A\beta_1^A$ $\beta_1^A = \text{Hb-H}$ $\gamma_1^F = \text{Hb-Bart's}$ δ_1^A	in reduced amount	As in β -thalassaemia; probably only heterozygotes survive	Thailand, China, Greece

Inborn errors of amino-acid metabolism

In alkaptonuria the absence of homogentisate oxygenase prevents the catabolism of homogentisic acid to maleylacetoacetic acid with the result that homogentisic acid accumulates and is excreted in the urine. The renal clearance of homogentisic acid is very high.

Phenylketonuria, histidinaemia and maple syrup urine disease (leucinosis) resemble alkaptonuria in that each is caused by the genetically determined absence of an enzyme and the consequent accumulation of the relevant substrate. In each case, however, the substrate undergoes 'abnormal' reactions because of its high concentration, for example in phenylketonuria the transamination of phenylalanine to phenylpyruvic acid or β -imidazolylpyruvic acid and reduction to the α -hydroxy acids. Substrates of the missing enzymes in abnormally high concentrations, as well as the abnormal

metabolites, are often toxic; they may cause brain damage in phenylketonuria and maple syrup urine disease, ochronosis and arthritis in alkaptonuria.

In albinism, though tyrosine is not converted to 3,4-dihydroxyphenylalanine (DOPA) and the latter is not converted to melanin, it is adequately metabolized by other pathways. The nature of the enzymatic defects in cystinosis, homocystinuria, hyperglycinaemia and oxalosis is still obscure.

Diseases arising from inborn errors of amino-acid metabolism are listed in Table 2. All involve some loss of survival fitness and many are virtually lethal. All are inherited as mendelian recessive characters, as would be expected in view of the fact that a mutant gene would tend not to survive if it produced a dominant character causing serious disability. Even recessively inherited lethal genes tend to vanish unless there is some compensating advantage to the heterozygote in some environments.

Table 2 Inborn errors of intermediary metabolism of amino acids

Condition	Defective enzyme	Biochemical features	Clinical features	Treatment	Reference
Alkaptonuria*	Homogentisate oxygenase	Urinary excretion of homogentisic acid	Urine darkens; ochronosis; arthritis in later life	None known	1,2
Phenylketonuria**	Phenylalanine 4-hydroxylase	Phenylalanine accumulates in blood, CSF, etc.; urinary excretion of phenylpyruvic acid and related compounds	Severe mental deficiency, epilepsy, abnormal EEG, eczema, behavioural disorders	Diet low in phenylalanine beginning at early age	2,3
Albinism***	<i>o</i> -Diphenol oxidase (tyrosinase)	Lack of melanin in skin, hair and eyes	Photophobia, nystagmus, carcinomata of the skin	None known	2,4

* Incidence 1 in 100 000. ** Incidence varies from 1 in 3200 to 1 in 10⁵ according to locality. *** Incidence 1 in 13 000.

Table 2 (continued) Inborn errors of intermediary metabolism of amino acids

Condition	Defective enzyme	Biochemical features	Clinical features	Treatment	Reference
cretinism (several types)	(1) Tyrosine iodinase (2) Coupling enzyme (3) Deiodinase	Lack of thyroid hormone	Cretinism, goitre	Thyroid, thyroxine or tri-iodothyronine	8
Maple syrup urine disease (leucinos)	Enzyme responsible for oxidative decarboxylation of α -ketoisocaproic, α -keto- β -methyl-valeric and α -keto-isovaleric acids	Leucine, isoleucine and valine accumulate in blood, CSF, etc.; urinary excretion of the 3 keto acids and related compounds	Cerebral degeneration; usually early death. Milder form with partial enzyme deficiency, symptomless except during infections, etc.	Diet low in leucine, isoleucine and valine	6
Cystinosis	Cystine reductase (?)	Cystine is deposited in reticulo-endothelial system, amino-aciduria, glucosuria, proteinuria, phosphaturia, dilute urine	Dwarfism, photophobia, renal acidosis, hypokalaemia, vitamin-resistant rickets; death before puberty. A benign (non-fatal?) variant occurs in adults	Palliative potassium salts, alkalis, vitamin D. Diet low in cystine and methionine (efficacy doubtful)	7
Homocystinuria	L-Serine dehydratase	Urinary excretion of homocystine	Mental retardation, retinal defects, dislocated lenses, malar flush, thromboses	Diet low in methionine, high in cystine. Pyridoxine	8
Hyperglycinemia (several types)	(Uncertain, depends on type)	Glycine accumulates in blood, etc.; urinary excretion of glycine and, in one type, methylmalonic acid	Neonatal lethargy and ketosis, neutropenia, hypoglobulinaemia, mental retardation	Diet low in protein	9
Oxalosis	Excessive conversion of glycine to oxalic acid	Calcium oxalate accumulates in kidneys, heart, bone marrow and cartilages	Nephrocalcinosis leading to progressive renal failure	None known	10
Histidinaemia	Histidine ammonia-lyase	Urinary excretion of β -imidazolylpyruvic acid and related compounds	Speech defects, mental retardation in some	Diet low in histidine	11
Familial tyrosinaemia (Uncertain)		Tyrosine level in blood and urine raised, urinary excretion of phenolic acids related to tyrosine, generalized amino-aciduria, glucosuria, fructosuria	Rapidly enlarging liver, jaundice, hypoproteinaemia, death common in infancy, survivors may have vitamin D-resistant rickets and acidosis	Diet low in tyrosine and phenylalanine (efficacy doubtful)	12
Hyperprolinaemia Type I Type II	Pyroline-5-carboxylate reductase Pyroline-5-carboxylate dehydrogenase	Hyperprolinaemia, urinary excretion of proline, glycine and hydroxyproline	Mental retardation, convulsions, renal disease, deafness	None known	13
Hydroxyprolinaemia	3-Hydroxy-pyroline-5-carboxylate reductase (?)	High levels of hydroxyproline in blood and urine	Mental retardation (?)	None known	13
Citrullinaemia	Argininosuccinate synthetase	High blood and urinary levels of citrulline, blood ammonia increased, urea excretion normal	Mental retardation, epilepsy, vomiting, ammonia intoxication	Diet low in protein	14, 15
Argininosuccinic aciduria	Argininosuccinate lyase	normal	normal	Diet low in protein	15, 16

Table 2 (concluded) Inborn errors of intermediary metabolism of amino acids

Condition	Defective enzyme	Biochemical features	Clinical features	Treatment
Hyperammonaemia Type I	Ornithine carbamoyl-transferase Carbamoyl-phosphate synthase	Blood ammonia about 10 mg/l; urea excretion normal	Mental retardation, ammonia intoxication	Diet low in protein (?)
Type II				

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Inborn errors of carbohydrate metabolism

Genetically determined absence of the appropriate intestinal enzyme causes inability to split lactose, sucrose or limit dextrin. Consumption of these substances may lead to diarrhoea and sometimes injury of the intestinal mucosa.

In galactosaemia, galactose is not converted to glycogen because of the absence of galactose-1-phosphate uridylyltransferase. Galactose 1-phosphate therefore accumulates and has a toxic effect due to its inhibition of phosphoglucomutase and other enzymes. Similarly, in fructose intolerance the absence of fructose-1-phosphate aldolase results in accumulation of fructose-1-phosphate, which causes severe hypoglycaemia, probably by inhibition of glucose-6-phosphatase. Defects in the metabolism of carbohydrates other than glycogen are listed in Table 3. With the exception of hereditary leucine-sensitive hypoglycaemia, all are probably or certainly inherited as mendelian recessive characters.

There are at least seven diseases due to an abnormality of glycoyl metabolism (Table 4). There may be failure to form this substance or a glycogen of abnormal structure may be laid down, or the glycogen deposited in various tissues may not be broken down normally. In six of the seven diseases a specific enzymatic defect has been demonstrated, but not all of these resemble typical inborn errors of metabolism in which a mutant gene fails to produce a normal enzyme. In idiopathic generalized glycogenosis there is a deficiency of α -glucosidase. In some, more severe, cases of GIERKE's disease glucose-6-phosphatase is absent from the liver, but more often it is present in diminished amount. A second enzyme, glucose-6-phosphate dehydrogenase, is also absent in some but not all persons with GIERKE's disease. Glucose-6-phosphatase deficiency and dextrin 1,6-glucosidase deficiency occur in the same families; in these families at least, the mutant gene is unlikely to be directly responsible for the enzymatic defects. The status of amylopectinosis and of hepatic glycogen phosphorylase deficiency is also somewhat uncertain.

Table 3 Inborn errors of metabolism of carbohydrates other than glycogen

Condition	Defective enzyme	Biochemical features	Clinical features	Treatment	Reference
Galactose diabetes	Galactokinase	Urinary excretion of galactose	Cataracts	Diet low in galactose from early infancy	1
Galactosaemia*	Galactose-1-phosphate uridylyl-transferase	Galactose and galactose 1-phosphate accumulate in tissues and body fluids	Liver damage, cataracts, mental deficiency, renal tubular dysfunction; often early death	Diet free from galactose	2
Fructose intolerance	Fructose-1-phosphate aldolase	Fructose and fructose 1-phosphate accumulate	Severe hypoglycaemia after ingesting fructose, sucrose, etc.	Avoidance of fructose and fructose precursors such as sucrose	3, 4
Fructosuria	Fructokinase	Urinary excretion of ingested fructose	Benign	Unnecessary	2

* Incidence 1 in 70 000.

Table 3 (continued) Inborn errors of metabolism of carbohydrates other than glycogen

Condition	Defective enzyme	Biochemical features	Clinical features	Treatment	Reference
Pentosuria*	L-Xylulose reductase	Urinary excretion of L-xylulose	Benign	Unnecessary	8
Alactasia	β -Galactosidase (lactase) in intestinal mucosa (lifelong)	Lactose not hydrolysed in small intestine	Diarrhoea; failure to gain weight	Avoidance of lactose	9, 7
Lactose intolerance	Probably intestinal β galactosidase (temporarily)	Lactose not utilized, lictosuria, amino-aciduria	Diarrhoea, possible death in infancy	Avoidance of lactose and sucrose	9, 7
Sucrose intolerance			Diarrhoea after ingesting sucrose, less severe diarrhoea after ingesting starch	Avoidance of sucrose, diet low in starch	7
Hereditary leucine-sensitive hypoglycaemia**	-	Hypoglycaemia accentuated by giving leucine or protein, through release of insulin	Hypoglycaemic convulsions, varying degrees of mental retardation, sometimes symptomless	Carbohydrates with every protein meal	8

* Incidence 1 in 50 000

** Inherited as a dominant character causing 40-60% of cases of idiopathic infantile hypoglycaemia

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Inborn errors of glycogen deposition or utilization

Condition	Clinical type	Biochemical features	Clinical features
Glucose-6-phosphatase deficiency (GLICKER'S disease)	1	Normal glycogen accumulates in liver and kidney	Hepatomegaly, hypoglycaemia, stunted growth with retarded bone age, etc
Idiopathic generalized glycogenosis (POMPE'S disease)	2	Normal glycogen accumulates in all organs	Cardiac failure, muscle hypotonia, neurological disorders, death in infancy
Dextrin 1,6-glucosidase (debrancher) deficiency (limit dextrinosis, FORBES' disease)	3	Abnormal glycogen with short branches deposited in liver and, sometimes, skeletal and cardiac muscle	Hepatomegaly, hypoglycaemia, less severe than GLICKER'S disease
α Glucan branching glycosyl transferase (brancher) deficiency (amylopectinosis, ANDERSEN'S disease)	4	Abnormal carbohydrate with long inner and outer branches deposited in liver, spleen and lymph nodes	Hepatic cirrhosis, death within two years of birth
Glycogen phosphorylase (glycogen phosphorylase of the muscle) deficiency (Mc ARTHUR'S syndrome)	5	Moderate accumulation of normal glycogen in skeletal muscles, lactate and pyruvate levels in blood fall during exercise	Generalized muscular fatiguability and pain
Glycogen phosphorylase (hepatic glycogen phosphorylase) deficiency (HERS' disease)	6	Normal glycogen accumulates in liver, phosphorylase content of liver and leucocytes reduced	Hepatomegaly, relatively benign
Deficiency of UDP-glucose-glycogen glucosyltransferase (glycogen synthetase)	-	Liver glycogen almost completely absent	Severe fasting hypoglycaemia

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Inborn defects of renal transport mechanisms¹

Many of the substances in the glomerular filtrate are normally reabsorbed with high efficiency in the proximal renal tubule. This active process requires specific receptor sites on the cells lining this region. One type of site absorbs cystine, lysine, arginine and ornithine. In cystinuria² these sites are absent or largely inactive, so that cystine, lysine, arginine and ornithine are very inefficiently reabsorbed from the glomerular filtrate and appear in the urine. Cystinuria is determined by a single pair of genes. Abnormal homozygotes excrete all four amino acids and tend to form cystine stones. Some heterozygotes excrete moderately increased amounts of cystine and lysine, others are completely normal.

In the Hartnup syndrome³ the renal tubular reabsorption of a different, and larger, group of amino acids is defective. Moreover, since absorption of tryptophan from the gut is also defective, bacterial metabolites of tryptophan are excreted in abnormal amounts.

There are several conditions characterized by one or more of the following: renal glucosuria⁴, phosphaturia⁵, renal acidosis⁶, generalized amino-aciduria⁷. Each is caused by loss of some specific function of the proximal renal tubule, often inherited in dominant fashion. With the exception of renal glucosuria, the tubular defect is associated with disease in some individuals. Phosphogluco-amino-aciduria⁸ (DENRÉ-DE TONI-FANCONI syndrome), 'benign amino-aciduria'⁹ and osteomalacia with amino-aciduria¹⁰ (adult FANCONI syndrome) were formerly considered to be separate entities, but the demonstration of renal loss of phosphate and bicarbonate in two cases of 'benign amino-aciduria'⁹ closed the gaps between it and the other two conditions. It seems probable that all three are manifestations of the same primary renal tubular defect¹¹, the clinical effects varying markedly from individual to individual, both in age at onset and severity. Cystinosis must be distinguished from these conditions since the progressive loss of renal tubular function in cystinosis is secondary to some more fundamental metabolic defect, as in galactosaemia and WILSON'S disease; these three diseases are recessively inherited.

Glycine is reabsorbed from the glomerular filtrate by a system probably specific for glycine. In glycinuria¹² this mechanism is defective; the condition is dominantly inherited.

In nephrogenic diabetes insipidus¹³ the distal tubule and collecting duct do not respond to vasopressin by becoming able to water.

In renal glucosuria and glucose-galactose malabsorption¹⁴ a disturbance of the reabsorption of glucose from the renal tu

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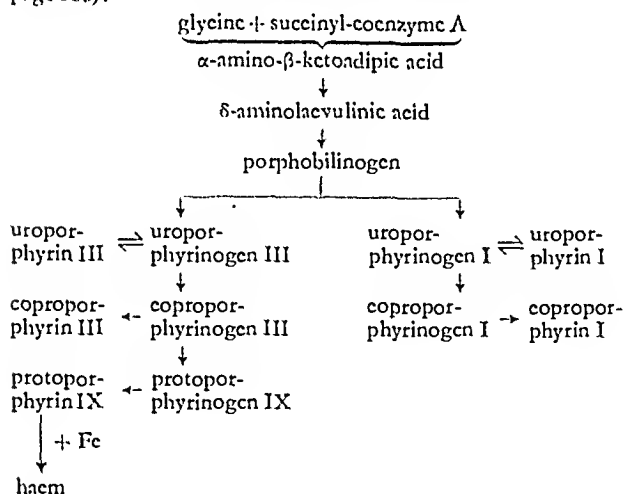
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Table 5 Some inborn defects of transport mechanisms

Condition	Site of defect	Biochemical signs	Clinical features	Treatment	Genetics
Cystinuria	Renal tubules and gut wall	Excessive urinary excretion of cystine, lysine, arginine and ornithine	Calculi of cystine in urinary tract. Often symptomless	High water intake, alkalinization; penicillamine	Two forms, both recessive
Hartnup disease	Renal tubules and gut wall	Delayed intestinal absorption of tryptophan, etc.; excessive urinary excretion of indoles and many amino acids	Cerebellar ataxia, photosensitive dermatitis	Nicotinamide	Recessive
Glucose-galactose malabsorption	Wall of intestine, renal tubules	Glucose, galactose and products of microbial fermentation in faeces; glucosuria	Diarrhoea; dehydration, sometimes fatal	Diet with fructose as sole carbohydrate	Autosomal recessive (?)
Glycinuria	Renal tubules	Glycine excretion increased	Probably benign	None known	Dominant
Renal glucosuria	Renal tubules	Glucosuria; reduced T_m (glucose) in type A; increased slope of glucose reabsorption curve in type B	Benign	None known	Dominant
Hypophosphataemia (phosphaturia)	Renal tubules	Urinary loss of phosphate	Rickets resistant to vitamin D; sometimes symptomless	Phosphate infusions; large doses of vitamin D or dihydroxycholesterol	Sex-linked with expression in most hemizygotes, some heterozygotes

Hyperbilirubinaemia¹ and porphyria²

Several inborn errors of the metabolism of pyrrole derivatives are known. The main stages of the synthesis of haem from glycine and succinyl-coenzyme A are as follows (for fuller details see page 355):



Complete failure of any of the enzymes leading to the formation of haem is incompatible with life since haem is an essential part not only of haemoglobin and myoglobin but also of a number of enzymes, especially the cytochromes. Deficiencies of the enzymes synthesizing haem can be due to inborn errors or the action of

toxic substances. Thus among other effects, lead poisoning inhibits the activity of the enzymes metabolizing δ -aminolaevulinic acid, so that the latter is excreted in the urine.

In the commonest forms (intermittent acute porphyria cutanea tarda hereditaria) the primary biochemical lesion is in the liver. These have been called respectively the Swedish and South African forms of hepatic porphyria, though both occur in other countries. Mixed porphyria and porphyria variegata are terms applied, in particular, to the form of porphyria cutanea tarda hereditaria common in South Africa.

Hepatic porphyria (or cutaneous hepatic porphyria) is caused by accumulation of porphyrins in the liver. The porphyrins so produced cannot be used for haem synthesis and are excreted via the bile. The condition can be acquired by alcohol or by ingestion of hexachlorobenzene, or as a result of liver disease.

Haem is normally broken down to bilirubin, which is conjugated with glucuronic acid in the liver and excreted as the conjugate in the bile. Free bilirubin in high concentration, in contrast to the conjugate, is toxic. Of the four known inherited conditions leading to hyperbilirubinaemia only one, the CRIGLER-NAJJAR syndrome, can be definitely attributed to the absence of an enzyme. The other three conditions may be the results of defects of a transport system.

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Table 7 Inborn defects of metabolism of pyrrole derivatives (hyperbilirubinaemia and porphyria)

Condition	Defective enzyme or system	Biochemical effects	Clinical features	Treatment	Incidence in genetics
Congenital non-haemolytic jaundice (CRIGLER-NAJJAR syndrome)	Bilirubin-glucuronic acid conjugating system	Serum bilirubin 150–400 mg/l (all free)	Severe kernicterus; often early death; sometimes symptomless	None known	Recessive
Constitutional hepatic dysfunction (GILBERT's disease)	Bilirubin-glucuronic acid conjugating system (?)	Serum bilirubin 10–30 mg/l (all free)	Probably harmless	None necessary	Probably dominant
Chronic idiopathic jaundice (DUBIN-JOHNSON syndrome)	Probably faulty hepatic excretion of pigment, etc. into the bile	Slight hyperbilirubinaemia (bilirubin all conjugated); unidentified brown pigment in liver parenchyma cells	Benign; sometimes liver enlargement and tenderness	None	Probably dominant
ROTOR syndrome	Possibly faulty hepatic excretion	Serum bilirubin 40–76 mg/l, half free and half conjugated; no pigment in liver	Some liver tests abnormal	None	Probably dominant
Congenital erythropoietic porphyria (GÜNTHER's disease)	Probably uroporphyrinogen isomerase	Uroporphyrin I and coproporphyrin I in tissues, plasma, urine and faeces	Often early death; photosensitization leading to severe scarring, erythrodontia; haemolytic anaemia	Splenectomy, protection from sunlight	50 known cases; recessive
Intermittent acute porphyria	Large amounts of δ -aminolaevulinic acid synthetase in liver	Porphobilinogen and δ -aminolaevulinic acid excreted in urine	Often intermittent; abdominal pain, neurosis and psychosis, peripheral neuritis, paralysis, generalized demyelination; mortality high	Avoidance of barbiturates	Incidence 0.015–0.1%; dominant

Table 7 (continued) Inborn defects of metabolism of porphyrin derivatives (hyperbilirubinaemia and porphyria)

Condition	Defective enzyme or system	Biochemical effects	Clinical features	Treatment	Incidence and genetics
erythra cruranea tarda hereditaria	Excessive hepatic porphyrin production	Faecal porphyrins high in excretion	Symptoms: sometimes mental symptoms	alcohol and barbiturates	
hepatoerythropoietic porphyria	Uncertain	Large amounts of coproporphyrin III in urine and faeces, amino-aciduria	Harmless	None	Rare; recessive
erythropoietic protoporphyria	Uncertain	Large amounts of protoporphyrin in erythrocytes, normoblasts and (sometimes) faeces	Relatively mild photosensitive dermatitis, erythema, itching, mild oedema	Avoidance of bright sunlight	Rare; dominant

Lipidoses¹

A group of pathological conditions, generally grouped together as 'lipidoses' are rather rare.

familial idiocy. However, it is not certain that the different forms of NEURONAL ceroid disease are genetically distinct, they may differ only in site and rate of lipid deposition, and this may also be true of metachromatic leucodystrophy.

References

Table 8 Lipidoses

Condition	Lipid accumulating	Site	Clinical features	Age at which symptoms appear	Genetics	Reference
GALICER'S disease (a) 'Adult' (b) Acute infantile (c) Juvenile and adult neurological	Glucocerebroside	Spleen, liver, bone marrow, leucocytes Brain in (b) and (c), lung in (b)	Splenomegaly, often gross, hepatomegaly; anaemia, bone disorder, purpura, cerebral degeneration in (b) and (c)	(a) 1-60 years (b) 1st or 2nd half year of life (c) 6-20 years	(a), (b) and (c) in different families, all recessive	1
TAYLOR'S disease (infantile amaurotic familial idiocy)	Ganglioside GM ₂ (G ₂), amino-glycolipid	White and grey matter of the brain	Cherry-red spot, progressive cerebral degeneration, death at age 1-5 years	Usually 4-6 months, sometimes earlier	Recessive	2
Juvenile and adult amaurotic familial idiocy				From 5 years onwards	Probably recessive	2

Table 8 (continued) Lipidoses

Condition	Lipid accumulating	Site	Clinical features	Age at which symptoms appear	Genetics
NIEMANN-PICK disease (a) Acute infantile (b) Cerebral juvenile (c) Noncerebral	Mainly sphingo- myelin	Spleen, bone marrow, liver; usually also brain and retina	Often cherry-red spot; hepatospleno- megaly; hepatic cir- rhosis; usually cere- bral degeneration and death in first 2½ years. Some adult cases are without neurological involvement	(a) From birth (b) Childhood (c) Up to 30 years or later	(a) Recessive (b) Recessive (c) Uncertain
Metachromatic leucodystrophy (a) Infantile (b) Adult	Sulphatides	Brain, kidney, urine, gall- bladder	(a) Cerebral and cere- bellar degenera- tion; spasticity; dementia; death after 1-6 years (b) Psychotic changes; blind- ness; aphasia; tetraplegia. Death after 3-12 years	(a) 1-2 years (b) Late child- hood or adulthood	(a) Recessive (b) Uncertain
Essential familial hyperlipaemia	Triglycerides, lipoproteins	Blood plasma (chylomicrons)	Hepatosplenomegaly; sometimes xantho- mata. Relatively benign	Usually early childhood	Complex
Hypercholesterolaemia	Cholesterol (free and esterified), phosphatides, sometimes tri- glycerides	Blood plasma (lipoproteins), tendons, skin, blood vessels	Cutaneous and tendi- nous xanthomata; atheroma of endocar- dium, coronary arter- ies or great vessels	From childhood onwards	Usually dominant

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- ² FREDRICKSON and TRAMS, in STANBURY et al. (Eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966, page 523.
- ³ FREDRICKSON, D.S., in STANBURY et al. (Eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966, page 586.
- ⁴ MOSER and LEES, in STANBURY et al. (Eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966, page 539.
- ⁵ FREDRICKSON and LEES, in STANBURY et al. (Eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966, page 429.
- ⁶ HARLAN et al., *Medicine (Baltimore)*, 45, 77 (1966).

Inborn errors of corticosteroid metabolism¹

Certain forms of adrenal hyperplasia have their origin in an inborn defect in the biosynthesis of steroids. The commonest is a defect in the hydroxylation of the steroid skeleton at C-21 due to a deficiency of steroid 21-hydroxylase, the result being a diminished synthesis of 21-hydroxysteroids. Since these steroids have no effect on the pituitary, the latter produces increased amounts of ACTH, resulting in further stimulation of the synthesis of 21-deoxysteroids. Some of these 21-deoxysteroids are precursors of androgens, the augmentation of which is the reason for the progressive virilization seen in these patients. When the deficiency of steroid 21-hydroxylase is very marked, practically no 21-hydroxysteroids are formed. This results in limitation also of aldosterone synthesis and the accumulation of progestogens, which act as aldosterone antagonists. The excretion of sodium by the kidneys is therefore increased, and in infants with this defect there is extreme loss of salt in the urine and possibly crises like those seen in Addison's disease.

A rarer form of inborn adrenal hyperplasia is due to deficiency of steroid 11 β -hydroxylase, resulting in increased formation of 11-deoxycorticosterone and excessive excretion of metabolites of this substance in the urine. Unlike patients with the defect of 21-

hydroxylation, such persons excrete only small amounts of ketosteroids in the urine and they show hardly any increased pregnanetriol. 11-Deoxycorticosterone causes sodium retention and this is probably the cause of the arterial hypertension in these patients.

Deficiency of 3 β -hydroxysteroid dehydrogenase is rare blocks the formation of progesterone from pregnenolone. The defect in 21-hydroxylation, the result is loss of salt in the but clinically the condition differs from inborn adrenal hyperplasia in the manner in which it affects differentiation of the genitalia in the foetus.

A case of deficiency of steroid 17 α -hydroxylase has been reported²; here the adrenal cortex produced excessive amounts of corticosterone and deoxycorticosterone, with consequent hypertension.

The various forms of inborn adrenal hyperplasia are each inherited through an autosomal recessive gene.

References

- ¹ SOFFER et al., *The Human Adrenal Gland*, Lea & Febiger, Philadelphia.
- ² STAMPEL and TOWKINS, in STANBURY et al. (Eds.), *The Metabolic Basis of Inherited Disease*, 2nd ed., McGraw-Hill, New York, 1966, page 635.
- ³ BIGLIERT et al., *J. clin. Invest.*, 45, 1946 (1966).

(For references see pages 460-461)

min A²nistry²

itamin A and the carotenes are soluble in fats, insoluble in water, easily oxidized. In the absence of oxygen they are stable to alkalis and heat. On the *cis-trans* isomerism of the carotenes vitamin A see ZACHARISSEN⁴. For structure and properties of vitamin A and related compounds see the table on pages 458-459.

ly

ological⁴ Mainly by the standardized growth test on vitamin A-deficient rats

hemical⁴ Spectrophotometrically in pure solution (vitamin A 8 m, carotenes at ca. 450 nm) or colorimetrically, for instance antimony trichloride (CARR-PRICE reaction), in biological material chromatographically after suitable extraction.

ts

Vitamin A, 1 International Unit (IU) = 0.344 µg *all-trans* vitamin A₁ acetate = 0.300 µg *all-trans* vitamin A₁, 1 US Pharmacopeia (P) Unit = 1 International Unit.

Carotenes 1 International Unit (IU) = 0.6 µg β-carotene, equivalent in activity to 1 IU vitamin A

genesis²

The carotenes are synthesized by the higher plants, algae and photosynthetic bacteria and are found in concentrated form in the proplasts. Acetate is converted by condensation and decarboxylation into isopentenyl pyrophosphate, from which a C₄₀ terpenoid compound arises by condensation. This substance gives rise by further condensation to a carotenoid precursor with 40 C-atoms, namely phytylene. The various carotenes arise by dehydrogenation, cyclization, isomerization, hydration and hydroxylation. Carotenes with a β-ionone ring are broken down in the animal organism to vitamin A, more probably by fission in the middle of the chain and by successive β-oxidation from the end of the isoprenoid in². In the liver oils, vitamin A is present in the esterified form

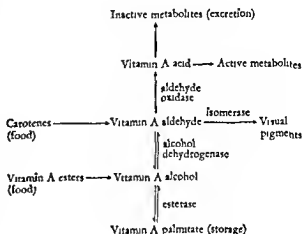
ake and excretion

In the USA the daily diet contains ca. 7500-10000 IU (2.3-3 mg) vitamin A¹². About a half of the apparent vitamin intake is in the form of the provitamin.

Carotenes are less easily absorbed than vitamin A and part of those in-

tration of tagged vitamin A to rats, radioactivity can be detected in the bile, urine and faeces⁴; the presence of vitamin A and/or its metabolites in bile points to enterohepatic circulation of the vitamin¹².

Metabolism of vitamin A



Function

Vitamin A is of great importance for maintenance of health and life, normal growth, the visual process and reproductivity. It appears to be necessary for the stability of the lipoprotein membrane

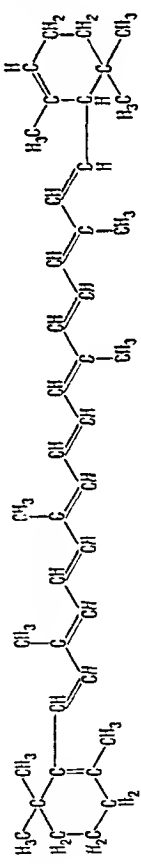
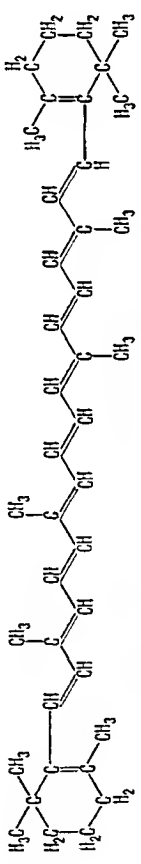
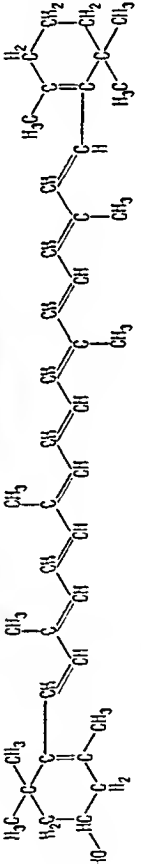
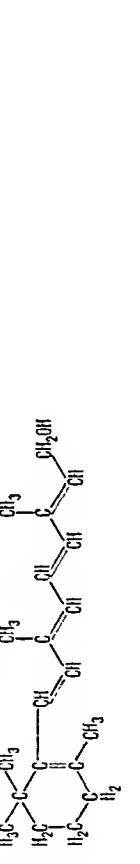
min A acid, while very active in maintaining growth, is not capable of maintaining reproductivity.

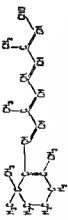
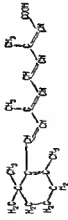

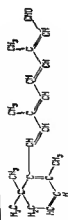
Metabolic functions of vitamin A²⁰

Active form	Biochemical reaction	Clinical effect
Vitamin A alcohol or other active form	Unknown	Reproduction in both sexes
Vitamin A aldehyde	Reaction with opsin	Visual process
Vitamin A acid or other active form	Liberation of proteolytic enzymes	Breakdown of cartilage
	Synthesis of mucopolysaccharides	Stimulation of mucous secretion in the epithelium
	Synthesis of corticosterone	Lesions in the adrenal cortex, interference with gluconeogenesis, deficiency states

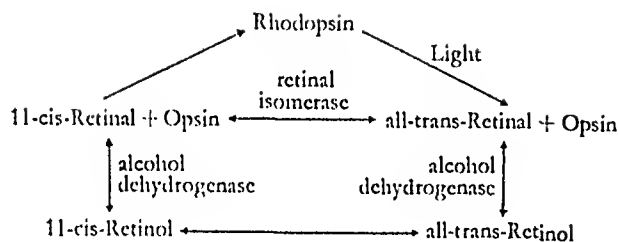
The vitamin A aldehydes retinal and dehydroretinal form together

Vitamin A is stored in the liver, the carotenes mainly in the fatty tissues. About 90% of the whole vitamin A of the body is stored in the liver; the liver reserves (up to 300 µg vitamin A per gramme liver¹³) are sufficient to meet the body's requirements of the vitamin for one year or more². These reserves, however, are rapidly used up in infections, hyperthermia and poisoning². 90-95% of the vitamin A in the liver is present as palmitate, the remainder as aldehyde and alcohol^{14, 15}. When any organ requires vitamin A, the stores in the liver are hydrolysed and the free alcohol transported by the blood to where it is required. In the tissues, particularly in the liver, vitamin A alcohol and aldehyde are rapidly oxidized to vitamin A acid; this substance is not stored, however, but rapidly broken down^{16, 17}. An active metabolite of vitamin A acid has recently been identified but its composition is unknown¹⁸. After adminis-

Names*	Formula and mol. wt.	Structure	Physical properties	Occurrence	Relative activity
α -Carotene	$C_{40}H_{56}$ 536.89		Violet to red crystals M.p. 187 °C (benzene/methanol)	Palm oil, mountain ash berries	50
β -Carotene	$C_{40}H_{56}$ 536.89		Violet to red crystals M.p. 180 °C	Plants, fruits	100
Cryptoxanthene (3-hydroxy- β -carotene)	$C_{40}H_{56}O$ 552.89		Red platelets M.p. 158 °C	Maize	50
Vitamin A ₁ (<i>all-trans</i>) (retinol*, axerophthol)	$C_{20}H_{30}O$ 286.46		Yellow prisms M.p. 62-64 °C	Liver of marine fish	100
9- <i>cis</i> -Vitamin A ₁ (10-a)	$C_{20}H_{30}O$ 286.46	As <i>all-trans</i> vitamin A ₁ but with double bond at C-9 in <i>cis</i> configuration	Yellow prisms M.p. 82 °C	-	21
11- <i>cis</i> -Vitamin A ₁ (10-b) (11- <i>cis</i> -retinol)	$C_{20}H_{30}O$ 286.46	As <i>all-trans</i> vitamin A ₁ but with double bond at C-11 in <i>cis</i> configuration	Orange-yellow oil	Retina	23

13- <i>cis</i> -Vitamin A ₁ (900- <i>a</i>)	C ₂₈ H ₄₄ O 286.66	A ₁ all <i>trans</i> vitamin A ₁ but with double bond at C-13 in <i>cis</i> configuration	Yellow prisms M.p. 58 °C	Fish liver	75
Vitamin A ₁ aldehyde (all <i>trans</i>) (retinal*, retin- aldehyde*, β-retinene, retinene)	C ₂₈ H ₄₄ O 284.45		Orange prisms M.p. 59 °C	Citrus fruits, green vegetables, liver	91
11- <i>cis</i> -Vitamin-A ₁ aldehyde (900- <i>b</i>) (11- <i>cis</i> retinal)	C ₂₈ H ₄₄ O 284.45	A ₁ all <i>trans</i> vitamin-A ₁ aldehyde but with double bond at C-11 in <i>cis</i> configuration	Orange prisms M.p. 64 °C	Eyes of crustacea	48
Vitamin-A ₁ carboxylic acid (all <i>trans</i>) (retinoic acid*)	C ₂₈ H ₄₂ O ₂ 300.44		Yellow needles M.p. 179 °C	Tissues?	~65
Vitamin A ₂ (3-dehydroretinol*)	C ₂₈ H ₄₂ O 284.45		Yellow needles M.p. 63-65 °C	Liver of freshwater fish	40
Vitamin A ₂ aldehyde (3-dehydroretinal*, 3-dehydroretinalde- hyde*, α-retinene, retinene)	C ₂₈ H ₄₀ O 282.43		Orange-red prisms M.p. 78 °C	Retina in fish	

* Trivial names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the International Union of Biochemistry [Biochem Supply Jista (Amst.), 107, 1 (1965)]



Vitamin A and carotene in their protein-bound form are thought to participate in an analogous manner in the sense of smell²⁴.

Requirements and deficiency symptoms

The requirement of vitamin A is proportional to the body weight. Daily requirements in health allowing for some reserve are 2500 IU vitamin A, 4000 IU carotene in fats, 7500 IU in green vegetables or 12000 IU in boiled carrots²⁶. In 10- to 15-year-old boys 1700 IU vitamin A are sufficient to maintain a plasma level of 300 µg/l²⁷. For infants from birth to 5 months it is assumed that exclusive breast-feeding can provide sufficient vitamin A²⁵. For recommendations of official bodies see the tables on pages 493-494.

Good sources of vitamin A are the fish oils (cod 1000, herring 5000, halibut and tunny 50000-100000 IU/g), liver, milk fat and egg yolk; green vegetables and carrots are rich in carotenes. See also pages 499-515.

Causes of vitamin A deficiency² are inadequate dietary intake, impaired absorption (fat deficiency) or storage, disturbances in the conversion of carotene into vitamin A, or rapid depletion of the body's reserves. Impairment of absorption or storage is seen in coeliac disease, cystic fibrosis of the pancreas, ulcerative colitis, pancreatotomy, obstruction of the biliary ducts and cirrhosis of the liver. Conversion of carotenes may also be impaired in diabetes and hyperthyroidism. Some infections result in disappearance of vita-

min A from the blood. The typical lesions of vitamin A deficiency are night blindness, xerosis or keratinization of various membranes (particularly xerophthalmia) and the formation of defective tissue and dentine during growth. The most sensitive test for vitamin A deficiency is measurement of dark adaptation of the eye; determination of vitamin A concentration in the serum is less reliable since the serum level does not fall until the body's reserve is fully depleted². In many countries of South America, Asia and Africa xerophthalmia is still one of the commonest causes of blindness in children^{29,30}. Other manifestations of vitamin A deficiency are Bitot's spots on the conjunctiva and roughness of the skin to hyperkeratosis of the hair follicles. In animals vitamin A deficiency has serious effects in pregnancy and is a cause of infertility and congenital deformities³¹.

Treatment and toxicity

Deficiency symptoms should be treated by giving vitamin A doses of up to 25000 IU (corresponding to ca. 30 ml liver oil). Xerophthalmia calls for initially higher doses (5000 IU/kg body weight daily for 5 days)^{29,30}. When liver oils are given in large doses, vitamin D may be ingested in toxic amounts, even though it has been shown that vitamin A in large doses diminishes the effect of vitamin D³².

Protracted treatment with high doses of vitamin A (for instance 100000 IU or more per day in children) may result in toxic symptoms such as anorexia, alopecia, affections of the skin and mucous swelling of the bones and diaphyses of the limbs, anaemia, enlargement of the liver and spleen and headache. All these symptoms are reversible and disappear rapidly on cessation of the treatment². Children overdosed with vitamin A may interfere with bone development and lead to premature fusion of the epiphyses³³.

In some countries vitamin A is given prophylactically to newborn children and infants in daily doses of 7500-10000 IU. Because of the danger of possible intoxication, however, it is better to restrict prophylactic doses to 2500 IU per day³⁴.

Acute vitamin A intoxication has been observed following consumption of polar bear liver, which contains 20000 IU per gramme^{35,36}; whale liver contains 4400 IU vitamin A per gramme; swine's liver only 100-150 IU per gramme³⁶.

Vitamin A deficiency symptoms in pregnancy and at various ages (modified from McLAREN and HALASA³⁰)


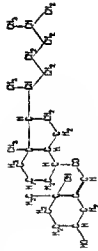
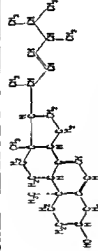
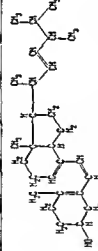
	Cause of deficiency	Symptoms
Pregnancy	Dietary carotene deficiency, increased requirement, depletion following repeated pregnancies	Low plasma level of vitamin A, low liver reserves, xerophthalmia (rare), Bitot's spots (occasionally)
Foetus		Low liver reserves, xerophthalmia (rare), abortion (?), congenital deformities (?)
Up to 12 months	Inadequacy of breast milk, low vitamin A content of breast milk, bottle feeding, infections	Low plasma level of vitamin A, depletion of liver reserves, xerophthalmia (fairly common), Bitot's spots (rare)
Up to 5 years	Breast feeding continued too long, dietary deficiency, infections	Commonest cause of conjunctival xerosis, xerophthalmia, Bitot's spots (occasionally)
School age	Dietary deficiency of carotene, vitamin A, fats and proteins	Conjunctival xerosis and Bitot's spots (main symptoms), night blindness, follicular hyperkeratosis (occasionally)
Adults	Dietary deficiency, infections, cirrhosis of the liver, pancreatic disease	Night blindness (main symptom), Bitot's spots (occasionally), xerophthalmia (rare), follicular hyperkeratosis (occasionally)

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Structure and properties of vitamin D and related compounds

Names*	Formula and mol. wt.	Structure	Physical properties	Occurrence	Antirachitic activity
Ergosterol	$C_{28}H_{44}O$ 396.66		M.p. 168 °C (with 1½ H ₂ O)	Yeast, ergot, hens' eggs	None (provitamin D ₂)
7-Dehydrocholesterol	$C_{27}H_{44}O$ 384.65		M.p. 150 °C (anhydrous)	Higher animals, man	None (provitamin D ₃)
22-Dihydroergosterol	$C_{28}H_{44}O$ 398.68		M.p. 152 °C	Synthetic	None (provitamin D ₄)
Vitamin D ₂ (ergocalciferol*)	$C_{28}H_{44}O$ 396.66		M.p. 115–118 °C	Formed by irradiation of ergosterol	In rats similar to, in chicks and apes less than that of vitamin D ₃
Vitamin D ₃ (cholecalciferol*)	$C_{27}H_{44}O$ 384.65		M.p. 84–85 °C	Formed by irradiation of 7-dehydrocholesterol. In fish-liver oils, egg yolk, milk	Antirachitic

Ketone 250	 $C_{28}H_{44}O_3$ 418.67	M.p 73 °C	Plants, fish-liver oils	One-tenth that of vitamin D ₃
Lumisterol	 $C_{28}H_{44}O$ 396.66	M.p 118 °C	Formed by irradiation of ergosterol	None
Tachysterol	 $C_{28}H_{44}O$ 396.66	Oil, readily oxidizing in air	Formed by irradiation of ergosterol	None (hypercalcaemic effect)
Dihydrotachysterol	 $C_{28}H_{46}O$ 398.68	M.p. 125-127 °C	Synthetic	400 times less active than vitamin D ₃ (same hypercalcaemic effect)

* Trivial names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the International Union of Biochemistry [Biochem Supply Asia (Amst.), 107, 1 (1965)].

- (b) FANCONI's syndrome
- (c) primary vitamin D resistance
- (d) renal insufficiency

The clinical symptoms of rickets are pain in the limbs, particularly the legs, genu valgum, bending of the long bones, thickening of the synchondroses of the ribs and of the joint epiphyses, and protuberance of the forehead. Tetany is also an occasional symptom. The radiological changes consist in widening of the epiphyses combined with disorganization of the epiphyseal disk, and appearance of a cup-shaped structure in place of the normal, distinct, straight boundary between metaphysis and epiphysis. The biochemical changes observed are slight lowering of the plasma calcium level, marked lowering of the plasma phosphate level, reduced urinary calcium excretion, increased phosphate clearance, increased phosphate excretion index and a rise in the plasma concentration of alkaline phosphatase; the calcium phosphate product in the plasma is lower than normal. One of the first signs of vitamin D deficiency is an increase in the amino-acid content of the urine²³.

Primary vitamin D-resistant rickets is congenital and usually hereditary. It is characterized by lower plasma phosphate levels and an increase in the phosphate excretion index. The vitamin D activity of the serum must be 10-20 times the normal value if the calcium metabolism is to be restored to normal²⁴. This form of rickets may be due to a defect of vitamin D metabolism^{25, 26} and excretion.

Treatment

Prophylaxis of rickets: Sun-baths or quartz lamp treatment, 400 IU vitamin D per day in the pure form or as cod-liver oil.

Treatment of rickets: Rickets and osteomalacia due to a simple deficiency of vitamin D respond to daily oral doses of 3000 IU vitamin D¹⁹; in premature infants and children with impaired absorption these should be given intramuscularly. Treatment with massive doses has the disadvantage that there is uncertainty as to the extent to which single high doses are absorbed. High vitamin D doses are called for in primary vitamin D-resistant rickets, and treatment should begin with 50 000 IU per day²⁶. Complete disappearance of the radiological and biochemical symptoms has been reported with a total of 5-400 million IU, depending on the individual²⁴. The maintenance dose, again depending on the individual, ranges from 1000 to 500 000 IU per day²⁴. If growth of the long bones is to proceed normally, treatment must be started immediately after birth²⁷.

Treatment of lupus vulgaris with vitamin D in very massive dosage is now usual only if other tuberculostatic drugs cannot be given.

Toxicology

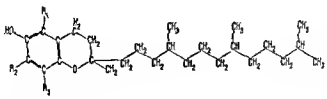
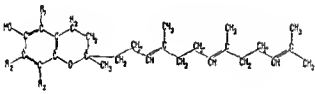
All the D vitamins are toxic in large quantities. High doses of vitamin D mobilize the bound calcium of the skeleton and bring about a considerable increase in the plasma calcium level as well as in the urinary excretion of phosphate and calcium. The calcium mobilized from the bones is taken up in the soft tissues, particularly the kidneys and media of the vessels. The clinical symptoms are loss of appetite, gastro-intestinal disturbances, pain in the head and joints and muscular weakness; in children other signs are a dry, loose skin, tremor of the limbs, loss of muscle tone with fibrillary spasms and arterial hypertension. When death occurs, this is usually due to renal failure. The symptoms of vitamin D poisoning are reversible when ingestion of the vitamin is stopped.

The toxic effect of vitamin D appears when daily doses exceed 1000-3000 IU per kg body weight and when these doses are given over several months; in infants, hypercalcaemia may appear even with total daily doses of 3000-4000 IU²¹. The clinical appearance of this idiopathic hypercalcaemia of infancy is very similar to that of vitamin D poisoning²⁸. For this reason, infants and pregnant women (since idiopathic hypercalcaemia may already occur in utero) should not be given more than 400 IU vitamin D per day^{21, 29}. Since enrichment of milk, margarine and baby foods with vitamin D is now quite common in many countries, the intake of this substance by infants and children is often excessive, for instance in the USA and Canada up to 2000 IU per day²¹, in England up to 1200 IU per day³⁰.

Vitamin D₂ is less suitable for treating rickets since its hypercalcaemic effect at high dosage is greater than that of vitamin D₃. Although dihydrotachysterol has only a very slight antirachitic activity it is, like vitamin D, capable of increasing the serum calcium level. The danger of poisoning is the same, however, with both substances. In the treatment of hypercalcaemia it is essential that the serum calcium level should be watched.

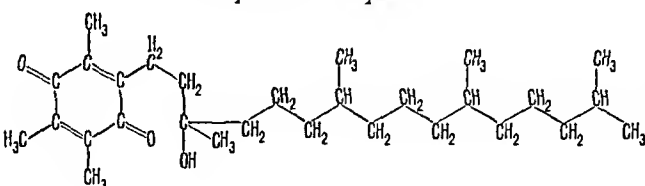
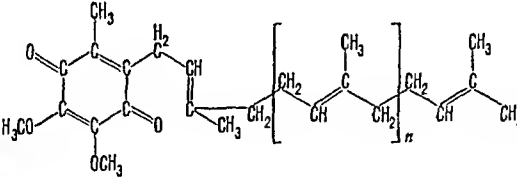
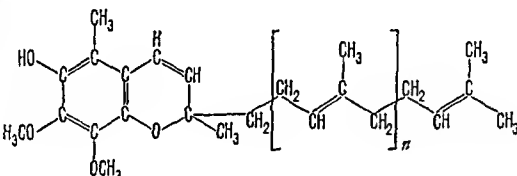
Vitamin E

Structure and properties of vitamin E and related compounds

Names*	Formula and mol. wt.	Structure	Main source	Activity
<i>Tocols</i>				
				
Tocol	$C_{55}H_{100}O_2$ 358.64	$R_1 = H, R_2 = H, R_3 = H$	Synthetic	Inac
8-Methyltocol (δ -tocopherol)	$C_{57}H_{104}O_2$ 402.67	$R_1 = H, R_2 = H, R_3 = CH_3$	Soybean oil	1
5,8-Dimethyltocol (β -tocopherol)	$C_{59}H_{108}O_2$ 416.69	$R_1 = CH_3, R_2 = H, R_3 = CH_3$	Wheat-germ oil	33
7,8-Dimethyltocol (γ -tocopherol)	$C_{59}H_{108}O_2$ 416.69	$R_1 = H, R_2 = CH_3, R_3 = CH_3$	Maize-germ oil	10
5,7,8-Trimethyltocol (α -tocopherol)	$C_{61}H_{112}O_2$ 430.72	$R_1 = CH_3, R_2 = CH_3, R_3 = CH_3$	Maize-germ oil, wheat-germ oil, etc., animal tissues	100
<i>Tocotrienols</i>				
				
8-Methyltocotrienol (δ -tocotrienol)	$C_{57}H_{100}O_2$ 396.62	$R_1 = H, R_2 = H, R_3 = CH_3$	Palm oil	
5,8-Dimethyltocotrienol (β -tocotrienol, β -tocotrienol)	$C_{59}H_{104}O_2$ 410.65	$R_1 = CH_3, R_2 = H, R_3 = CH_3$	Wheat	5
7,8-Dimethyltocotrienol (γ -tocotrienol)	$C_{59}H_{104}O_2$ 410.65	$R_1 = H, R_2 = CH_3, R_3 = CH_3$	Rice	
5,7,8-Trimethyltocotrienol (α -tocotrienol, α -tocotrienol, tocotrienol-3)	$C_{61}H_{108}O_2$ 424.67	$R_1 = CH_3, R_2 = CH_3, R_3 = CH_3$	Wheat	30

*Tocyl names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the I.U.

Structure and properties of vitamin E and related compounds (continued)

Names*	Formula and mol. wt.	Structure	Main source
<i>Tocopherol-like compounds</i>			
α -Tocopherylquinone (α -tocopherolquinone)	$C_{29}H_{50}O_3$ 446.72		Oxidation product of α -tocopherol, green plants
Ubiquinones (coenzymes Q)		 $n = 4-8$	Ubiquinone-9 (ubiquinone-45, coenzyme Q ₉)*: leaves; ubiquinone-10 (ubiquinone-50, coenzyme Q ₁₀)*: liver, yeast
Ubichromenols		 $n = 5-8$	As corresponding ubiquinones
* Trivial names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the national Union of Biochemistry [<i>Biochim. biophys. Acta (Amst.)</i> , 107, 1 and 5 (1965)].			
** Relative activity in antisterility test on rats.			

that the process resembles the synthesis of the ubiquinones (formation of the terpenoid chain of mevalonic acid and of the aromatic ring from phenylalanine)¹².

Intake and excretion

The daily intake of adults in the USA has been estimated at 24 mg total tocopherols and 14 mg α -tocopherol¹³, by another authority at 7.4 mg α -tocopherol¹⁴. The tocopherol esters are hydrolysed in the small intestine, and bile is necessary for their absorption. Probably only about 35% of the tocopherols in food is absorbed, the remainder being excreted in the faeces¹⁵. The normal concentration in adult serum is ca. 10 mg/l, in newborn infants ca. 5 mg/l (see page 609). The maximum blood level is reached 4-9 hours after giving tocopherols^{16,17}.

α -Tocopherol is stored in the liver and fatty tissues. High concentrations occur in the pituitary, adrenals, uterus and testes¹⁸. In the liver, tocopherol has been found in the mitochondria and microsomes¹⁶. The amount of tocopherols stored by the body is several grammes². In the fatty tissues this is believed to include also α -tocopherylquinone, an oxidation product of α -tocopherol¹⁹.

The metabolites tocopheronic acid and tocopheronolactone have been isolated in the form of glucuronides (SMON metabolite)²⁰ from the urine of persons given large amounts of tocopherol.

Function

The tocopherols act as antioxidants in the following processes both in vitro and in vivo^{21,22}:

- they prevent the oxidation of unsaturated fatty acids (linoleic acid) to peroxides; lipoperoxides are associated with the formation of the yellowish brown pigment in smooth muscle (ceroid pigment)
- they prevent the oxidation of vitamin A and the carotenes
- they prevent the oxidation of thiol groups, particularly in enzymes, presumably in conjunction with selenium²².

The relationship between vitamin E and cholesterol metabolism is obscure²². The tocopherols may play a role in nucleic acid metabolism²⁴ and in erythropoiesis²⁵. There may be a functional con-

nection between the tocopherols and the ubiquinones, which are involved in electron transport²⁶, and the formation of adenosine triphosphate (see page 403)²⁷. Vitamin E seems to have a role in the transport and metabolism of vitamin B₁₂²⁸.

Requirements and deficiency symptoms

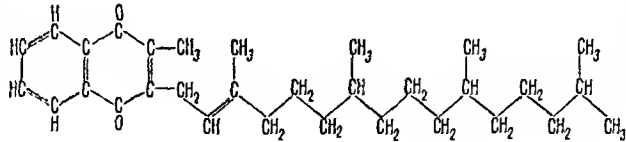
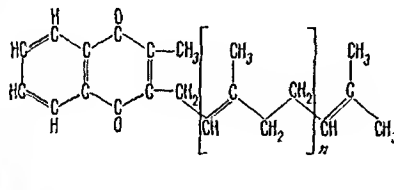
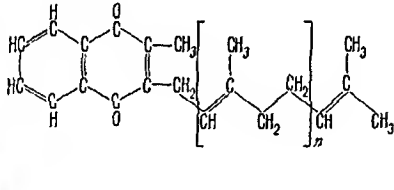
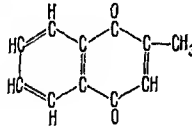
Healthy adults require 10-30 mg α -tocopherol per day (also page 494), depending on the intake of polyene fatty acids. 0.6 mg α -tocopherol at least being required per gramme of fatty acid²¹. The minimal requirement of infants is probably per kg body weight³², an amount normally absorbed with the milk.

Vegetable oils are rich in tocopherols, especially wheat-germ oil with 200-300 mg/100 g. Other good sources of tocopherol are cereals and eggs. Animal tissues contain little tocopherol, as α -tocopherol.

Vitamin E deficiency results in various changes depending on species, age and nutritional state. They include impaired reproduction and absorption of the foetus (rats, mice, guinea-pigs), muscular dystrophy accompanied sometimes by marked cerebellar atrophy (monkeys, mice, etc.), formation of ceroid pigments (mice, swine), increased haemolysis in vitro (rats, chickens), phthalomycin (chickens), exudative diathesis (chickens), necrosis of the liver ('respiratory decline' in rats), renal autolysis (rats). In human beings the signs of vitamin E deficiency are not marked.

A measure of the vitamin E status is provided by the per cent haemolysis test³³. In many persons a lowered serum tocopherol level is associated with an increase of in vitro haemolysis³⁰. A low serum level is common in newborn infants and particularly in premature infants, and vitamin E deficiency is a possible cause of neonatal anaemia³⁴ and haemolytic anaemia³⁵ in infants. Vitamin E deficiency may also be caused by impaired absorption of fat. Thus low tocopherol serum levels, often combined with cerebellar atrophy and the deposition of ceroid pigments in the smooth muscle (of the intestinal tract), have been observed in sprue, coeliac disease, cirrhosis, pancreatitis and particularly cystic fibrosis of the pancreas. A definite relationship between muscular dystrophy and vitamin E deficiency has been suggested.

Structure and properties of vitamin K and related compounds

Names*	Formula and mol. wt.	Structure	Physical properties	Occurrence	Act.
Vitamin K ₁ (30) (phyllo-quinone*)	C ₃₁ H ₄₆ O ₂ 450.71		Yellow oil M.p. -20 °C	Green plants, tomatoes, some bacteria. Isolated from alfalfa	100
Vitamin K ₂ (30) (mena-quinone-6*)	C ₄₁ H ₅₆ O ₂ 580.90	 $n = 5$	Yellow crystals M.p. 50 °C	Isolated from putrid fishmeal	100
Vitamin K ₂ (36) (mena-quinone-7*)	C ₄₆ H ₆₄ O ₂ 649.02	 $n = 6$	Yellow crystals M.p. 54 °C	Some bacteria. Isolated from putrid fishmeal	70
Menadione (vitamin K ₃ , methyl-naphtho-quinone)	C ₁₁ H ₈ O ₂ 172.19		Yellow needles M.p. 106 °C	Synthetic. Possibly a metabolite	ca. 100

* Trivial names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the International Union of Biochemistry [*Biochim. biophys. Acta (Amst.)*, 107, 5 (1965)].

** Relative activity in vitamin K-deficient chicks.

in some intestinal complaints like severe diarrhoea¹⁵ and steatorrhoea¹⁶, as well as in impaired absorption of the vitamin due to lack of bile (biliary fistula, obstruction of the bile ducts). The hypoprothrombinaemia associated with severe injury to the liver parenchyma is not due, however, to vitamin K deficiency and is also not reversed by administration of the vitamin; this forms the basis of a test of liver function. Vitamin K deficiency can also occur during long-term treatment with antibiotics or sulphonamides as a result of destruction of the intestinal flora.

During the first days of life the prothrombin activity of the plasma is 10–50% of that in adults¹⁷, possibly because the intestinal flora is not sufficiently developed and intake of the vitamin with milk is small. Among newborn infants not given vitamin K, 0.1–1% suffer from bleeding, a proportion that has been shown to be reducible by vitamin K treatment^{18,19}.

Treatment

Vitamin K is given prophylactically to newborn infants, particularly premature infants and those with anoxia, the dosage of the vitamin (or of a water-soluble preparation) being 0.5–1 mg subcutaneously or intramuscularly or 1–2 mg orally at birth¹⁸. Double these doses may be necessary in children whose mothers have been treated with anticoagulants. Administration of the vitamin to mothers ante partum is not recommended²⁰. The prophylactic use of the water-soluble menadione derivatives in pregnant women and newborn children is inadvisable on account of the danger of hyperbilirubinaemia and an increased tendency to kernicterus; these effects may be due not to the menadione derivatives themselves but to their intermediary metabolites.

The vitamin is given to correct low prothrombin activity due to a deficiency (see under 'Requirements and deficiency symptoms', above) as well as to overdosage of anticoagulants.

If possible, vitamin K should be given by the oral, intramuscular or subcutaneous route and not intravenously²¹.

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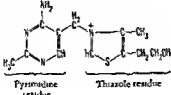
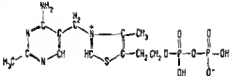
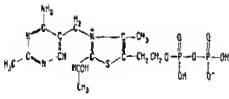
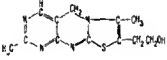
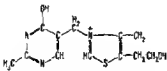
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Thiamine

(For references see page 471)

nine¹⁻³

re and properties of thiamine and related compounds:

Compound	Formula and mol wt.	Structure	Physical properties	Occurrence and activity
thiamine (vitamin B ₁ , ermin)	C ₁₂ H ₁₇ N ₄ OS (cation) 265.36 C ₁₂ H ₁₆ N ₄ OSCl ₂ (hydrochloride) 337.27		Colourless needles, readily soluble in water, odourless when pure, thermolabile in neutral and alkaline solution, stable to atmospheric oxygen, unstable to oxidizing agents and ultraviolet light M p. 245-248 °C (hydrochloride)	Plants In an tissues as thia- mine pyrophos- phate
thiamine diphosphate (IDP) thiamine triphosphate (TTP) acetoxymethyl- thiamine	C ₂₂ H ₃₂ N ₄ O ₇ P ₂ S 424.31		Pale yellow needles, readily soluble in water M. p. 242-244 °C	Animal tissue Cofactor of decarboxylat- ion and other enzymes
hydroxy- methyl-2-thia- mine diphos- phate hydroxy- methyl-2-thia- mine pyro- phosphate	C ₂₂ H ₃₃ N ₄ O ₇ P ₂ S 468.37			Micro-organ- isms, repres- ent 60% of the thiamine in <i>E. coli</i> 4 Also known as 'at acetaldehyde' (see page 39)
thiochrome	C ₁₂ H ₁₆ N ₄ OS 262.34		Yellow prisms showing blue fluores- cence in solution M p. 277-278 °C	Oxidation product of thiamine
xythiamine	C ₁₂ H ₁₆ N ₄ O ₄ S 266.34		M p 195-200 °C	Antagonist of thiamine

say

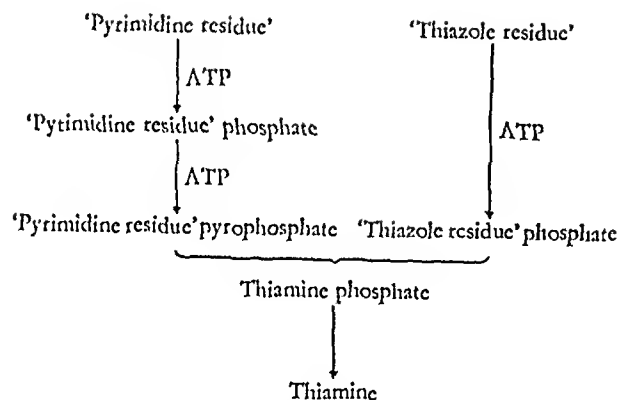
Biological Rat protection test, rat growth test, now little used
Microbiological Thiamine with *Ochromonas malhamensis* 5 or *Ochromonas danica* 6 pyrimidine and thiazole residues with *Saccharomyces cerevisiae* 7

Fluorimetric With apodecarboxylase from yeast 8
Chemical 9 Quantitatively in pure solution by titration of the
ionide, gravimetrically as reineckate, colorimetrically via the *azo*
derivatives from thiamine and d ironium salts, fluorimetrically
th cyanogen bromide, in biological material by oxidation of thia-
mine to thiochrome, which shows strong blue fluorescence in ultra-
violet light, with suitable modifications the thiochrome method can
used to determine the mono-, di- and triphosphates of thiamine
well as the protein bound thiamine

Units

No international unit, by weight The former International
(= 0.001 mg thiamine hydrochloride = the U.S. Pharmac
Unit) is now obsolete

B₁



Thiamine, but not thiamine phosphate, is converted by ATP into thiamine pyrophosphate (for instance in yeast and intestinal tissue). ATP can also convert thiamine pyrophosphate into thiamine triphosphate (yeast). On the activation of aldehydes by thiamine pyrophosphate see under 'Function', below.

Intake and excretion

In the USA, the daily diet contains about 2.15 mg thiamine¹¹, in Germany about 1.8 mg¹². Thiamine is readily absorbed in the small intestine and converted enzymatically in the intestinal mucosa into thiamine pyrophosphate. In rats, thiamine is synthesized by the intestinal flora¹³, but in man it is unlikely that bacterial synthesis plays an important role.

In whole blood the thiamine content is 20–75 µg/l, in serum 18–62 µg/l, in spinal fluid 3–12 µg/l¹⁴. Erythrocytes contain 80 µg/l, leucocytes 675 µg/l¹⁴. The thiamine content of the serum in newborn children is very high (see page 609). Small amounts of free thiamine are present in the serum, whereas in the erythrocytes and tissues the main component is thiamine pyrophosphate. The presence of thiamine monophosphate and triphosphate and thiochrome in the tissues has often been reported¹⁵. The heart muscle is fairly rich in thiamine (2–3 µg/g), as are the brain, liver and kidneys (1 µg/g); smaller quantities are present in the skeletal muscles (0.5 µg/g)¹⁶. The human liver contains about 4 mg of thiamine¹⁷.

When the daily dietary intake of thiamine rises above 0.5–0.6 mg the urinary excretion of the vitamin increases in proportion to the intake; on an ample diet it amounts to at least 100 µg/day^{2,18} (see also page 676). The urine also contains breakdown products (pyrimidine and thiazole residues) the amounts of which are not proportional to the thiamine content of the diet, so that they are regarded as a measure of the rate at which body stores of thiamine are being depleted¹⁹. The thiamine content of breast milk (see page 689) depends on the thiamine intake and shows large individual variations.

Function

Thiamine pyrophosphate possesses coenzyme functions in the breakdown of carbohydrates (oxidative decarboxylation of pyruvate, see page 391), in the citric acid cycle (oxidative decarboxylation of α -ketoglutarate, see page 390), in the pentose phosphate cycle (transketolase reaction, see page 421) and other biochemical reactions²⁰; at least 24 enzymes are known that contain thiamine pyro-

phosphate as coenzyme². The active aldehyde group in thiamine is formed or transported by thiamine pyrophosphate and is bound to the C-2 atom of the thiazole ring (see table).

Thiamine pyrophosphate plays an important part in the conduction of stimuli in the peripheral nerves and in the recovery after stimulation²³; during stimulation of the *peripheria* thiamine is liberated from thiamine pyrophosphate²⁴.

The thiamine-sparing effect of dietary fats probably derives from the fact that in thiamine deficiency the activity of pyruvate decarboxylase is more rapidly inhibited than that of oxoglutarate decarboxylase (α -ketoglutarate dehydrogenase)²; in thiamine deficiency, however, toxic products may also be formed from carbohydrates.

Various synthetic compounds resembling thiamine in structure, such as oxythiamine, pyriothiamine and neopyriothiamine, are thiamine antagonists²⁵; antithiamine factors of unknown origin occur in bacteria, plants and animals (particularly in cold-blooded animals, where the antimetabolite concerned is also known as 'thiaminase')²⁶.

Requirements and deficiency symptoms

The requirement of thiamine depends primarily on the intake of carbohydrates, although in practice it is usually related to the total energy intake. In adults the minimum requirement is about 0.27–0.36 mg per 1000 kcal²⁸. In bottle-fed infants the maintenance dose is given as 0.14–0.20 mg per day²⁹. The Joint FAO/WHO Expert Group²⁷ recommends a daily thiamine intake of 0.4 mg per 1000 kcal for infants, children, adults and pregnant and lactating women (see page 493). The allowances of the Food and Nutrition Board (USA)²⁹ (see page 494) are based on a daily intake of 0.5 mg per 1000 kcal. The requirement of thiamine increases with the metabolic rate. The possible presence of antithiamine factors in the diet must also be allowed for.

Good sources of thiamine are yeast, pork, liver, kidney, wholemeal cereals (see pages 507–508). The vitamin is destroyed during cooking, particularly in alkaline media, but is not affected by deep freezing¹.

The classical symptoms of vitamin B₁ deficiency are anorexia, nausea and vomiting. Other symptoms are fatigue, weakness, hypotonia of the gastrointestinal tract and disturbances of peripheral nerves (weakness in the limbs, hyperaesthesia and paraesthesia, disturbances of coordination). Emotional disturbances are also observed, such as depression, irritability and impaired memory and power of concentration.

Beriberi takes various forms according to the predominant symptoms:

(a) An exudative form, in which oedema is the first symptom. This may be followed by enlargement of the heart and right heart failure with sudden death.

(b) A 'dry' form in which the main symptoms are polyneuritis of peripheral degenerative type and atrophy of the muscles of the limbs. In European latitudes thiamine deficiency is marked by polyneuritis; it is seen for example in chronic alcoholism, though this condition is probably accompanied in general by deficiency of several of the B vitamins³⁰.

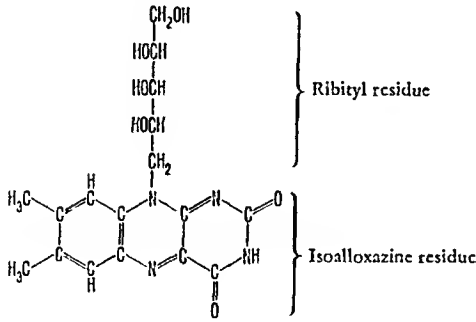
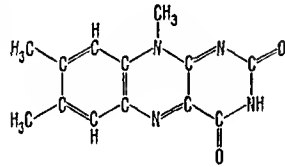
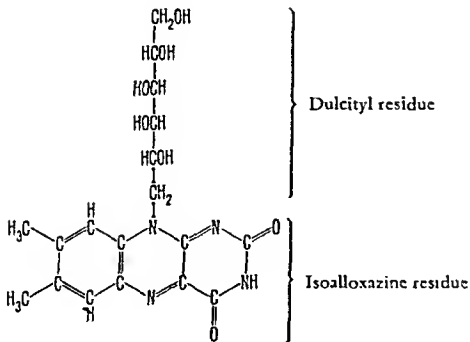
(c) A rare cerebral form with the symptoms of WERNICKE'S disease, namely nystagmus, ocular paralysis and emotional disturbance (irritability, sleeplessness, loss of memory, disorientation, hallucinations), followed by loss of consciousness and death. This disease is seen for instance in Europe among chronic alcoholics and occasionally in patients with cancer.

(d) An infantile form seen in the first year of life and a probable cause of the high infant mortality in southern and southern Asia; thus between 1954 and 1958 in the Philippines 15 000 children died each year from beriberi³¹. The chronic form is manifested by slow growth rate, constipation, vomiting and oedema, the acute form by heart failure and death. Occasionally the symptoms resemble those of meningitis or encephalitis. The cause of this vitamin deficiency disease is still to some extent obscure. In most cases the mother suffers from thiamine deficiency so that the maternal milk is deficient in this vitamin; toxic substances in the milk may play a role³².

Biochemically, thiamine deficiency is characterized by a low concentration of the vitamin (in beriberi 0–14 µg per 24 h) and by disturbances of carbohydrate metabolism (increased blood pyruvate and α -ketoglutarate levels³³) and by a low tissue concentration of thiamine pyrophosphate (erythrocytes³⁴, brain³⁵). The thiamine pyrophosphate content of the erythrocytes can be measured by means of the transketolase activity, which in thiamine deficiency can be normalized by administering thiamine pyrophosphate. The biochemical changes precede the pathological symptoms.

Reaction	Active aldehyde
Oxidative decarboxylation of pyruvate	Active pyruvate (α -lactyl-2-thiamine pyrophosphate) ²¹
	Active acetaldehyde (α -hydroxyethyl-2-thiamine pyrophosphate) ²¹
Oxidative decarboxylation of α -ketoglutarate	Active α -ketoglutarate (?)
	Active succinate semialdehyde (?)
Transketolase reaction	Active xylulose 5-phosphate (?)
	Active glycolaldehyde ²¹
	Active sedoheptulose 7-phosphate (?)
Glyoxylate carboxylase reaction	Active glyoxylate ²²
	Active formaldehyde ²²
	Active tartronic semialdehyde ²²

Structure and properties of riboflavin and related compounds

Names	Formula and mol. wt.	Structure	Physical properties	Occurrence and
Riboflavin (vitamin B ₂ , lactoflavin, 7,8-dimethyl-10-[D-ribityl]-isoalloxazine)	C ₁₇ H ₂₀ N ₄ O ₆ 376.37		Orange-yellow needles, bitter taste, slightly soluble in water and ethanol, readily soluble in acids, stable to heat when dry and to acid media, very unstable to alkalis and light. Yellowish green fluorescence in solution M.p. 275–282 °C (decomp.)	Constituent of flavin mononucleotide, flavin adenine dinucleotide. Occurs free form in some micro-organisms. Makes up 0.5–2% of total riboflavin in animal organs ⁴ . Present in urine
Flavinmononucleotide (FMN) (riboflavin-5'-phosphate)	See page 345	See page 345	Yellow powder, soluble in water	In micro-organisms as active group of flavoproteins, and plants and animals. Makes up 5–30% of total riboflavin in animal organs ⁴
Flavinadenine dinucleotide (FAD)	See page 345	See page 345	Yellow powder, readily soluble in water, insoluble in ethanol	In micro-organisms as active group of flavoproteins, and plants and animals. Makes up 70–90% of riboflavin in animal organs ⁴
Lumiflavin (7,8,10-trimethyl-isoalloxazine)	C ₁₃ H ₁₂ N ₄ O ₂ 256.27		Yellow crystals, only slightly soluble in water. Blue fluorescence in solution M.p. 333 °C (decomp.)	Formed from riboflavin by irradiation in alkaline solution. Antagonist of riboflavin
Galactoflavin (7,8-dimethyl-10-[D-dulcitol]-isoalloxazine)	C ₁₈ H ₂₂ N ₄ O ₇ 406.40		Yellow crystals, slightly soluble in water	Antagonist of riboflavin

per day, 10% of the intake is excreted; with an intake of 1.5 mg, about 20% is excreted, with an intake of 5–11 mg, about 60%^{17,19} (see also page 676). The concentration of riboflavin in breast milk depends on the intake of the vitamin²⁰.

Function

In the form of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) riboflavin forms the active group of the flavoproteins, enzymes with an important function in biological oxidations (see pages 402–403). Here the isoalloxazine system acts as a reversible redox system. In the oxidized form (fluorescent) the flavoproteins take up two hydrogen atoms and pass into the leucoform (non-fluorescent); in some reactions they take up only one hydrogen atom and become semiquinones. At least 40 flavoproteins

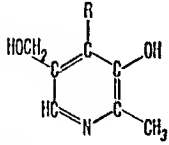
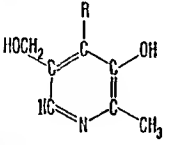
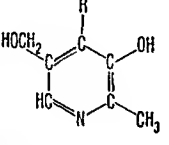
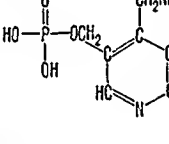
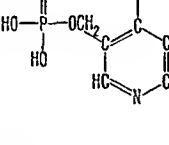
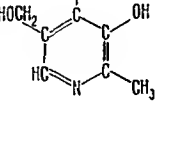
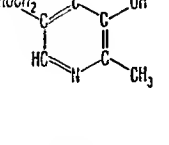
are known²¹, among them (active group in brackets) important oxidases such as aldehyde oxidase (FAD), xanthine oxidase (FAD), L-amino acid oxidase (FMN), D-amino acid oxidase (FAD), and hydrogenases like acyl-CoA-dehydrogenase (FAD) and succinate dehydrogenase (FAD), NAD(P)H₂ dehydrogenases (FAD), and glutathione reductase (FAD).

Riboflavin, in combination with protein, is necessary to prevent recurrent skin lesions such as those occurring in the corners of the mouth¹. In erythropoiesis, it is possibly necessary for the formation or effective functioning of erythropoietin²².

Requirements and deficiency symptoms

The requirement of riboflavin is usually based on the energy requirement²³ but can also be related to the protein requirement²⁴

Structure and properties of vitamin B₆ and related compounds

Names*	Formula and mol. wt.	Structure	Physical properties	Occurrence and
Pyridoxine*, pyridoxol* (adermine)	C ₈ H ₁₁ NO ₃ 169.18	 $R = -CH_2OH$	Colourless crystals, water-soluble, stable to heat, unstable to light M.p. 160 °C	Particularly in Vitamin B ₆ act for higher plant yeasts; only slight activity for bac
Pyridoxamine*	C ₈ H ₁₃ N ₂ O ₃ 168.20	 $R = -CH_2NH_2$	Colourless crystals, water-soluble, unstable to heat and light M.p. 193 °C	Particularly in tissues. Vitamin activity for mic organisms and h animals
Pyridoxal*	C ₈ H ₉ NO ₃ 167.17	 $R = -CHO$	Colourless crystals, water-soluble, unstable to heat and light	Particularly in a tissues. Vitamin activity for micr organisms and h animals
Pyridoxamine phosphate	C ₈ H ₁₃ N ₂ O ₅ P 248.18	 $R = -CH_2NH_2$	—	Coenzyme in transaminations
Pyridoxal phos- phate (codecarboxylase)	C ₈ H ₁₀ NO ₅ P 247.15	 $R = -CHO$	Yellow crystals, water-soluble M.p. > 270 °C	Particularly in muscle. Coenzyme in decarboxylation transaminations and phosphorylations
Pyridoxic acid (4-pyridoxic acid)	C ₈ H ₉ NO ₄ 183.17	 $R = -COOH$	White crystals, moderately soluble in water M.p. 247 °C	Particularly in uri (breakdown prod- uct). No vitamin activity
Deoxypyri- doxine	C ₈ H ₁₁ NO ₂ 153.18	 $R = -CH_3$	—	Vitamin B ₆ antag- onist in micro- organisms and animals

* Trivial names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the International Union of Biochemistry [*Biochim. biophys. Acta (Amst.)*, 107, 1 (1965)].

and excretion

verage daily diet contains about 2 mg vitamin B₆. Vitamin B₆ is probably hydrolysed in the intestine by phosphatases¹⁹, and the non-phosphorylated compounds undergo absorption in the upper intestinal tract. Vitamin B₆ is formed by the intestinal flora, though it is hardly likely that the body use of this source of the vitamin¹⁰. Excretion of vitamin B₆

leucocytes². The human body can apparently convert a maximum of 7 mg pyridoxine per day into pyridoxal phosphate, higher doses of pyridoxine do not cause any further increase in the pyridoxal phosphate in the body²⁰.

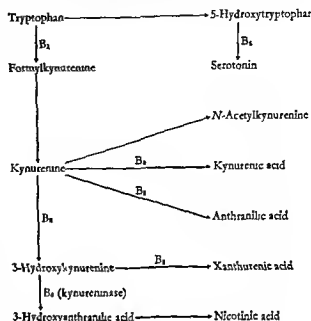
pyridoxal phosphate in the body appears to be bound to a glucan phosphorylase in the muscles¹⁸. The daily turnover of vitamin B₆

vitamin B₆

vitamin B₆ is involved as coenzyme in over 40 enzymatic reactions¹⁸. Pyridoxamine phosphate and pyridoxal phosphate act as coenzymes in transamination reactions important for the breakdown of γ -aminobutyric acid in the brain and for oxalic acid metabolism. Pyridoxal phosphate is the coenzyme in the decarboxylation of amino acids and for other reactions of amino acids (see table below). Pyridoxal phosphate is also involved in various reactions of tryptophan metabolism (see figure), and this fact is of use in the tryptophan loading test for diagnosis of vitamin B₆ deficiency²⁰. Pyridoxal phosphate is also the coenzyme in the transport of one-carbon units from serine to tetrahydrofolic acid²¹, plays a role in the formation of circulating antibodies²². It is involved with other cofactors in the synthesis of δ -aminolevulinic acid, a precursor of the porphyrins (haemopoiesis)²³. Pyridoxal phosphate is a component of a glucan phosphorylase¹⁸. It is un-

Dependence of tryptophan metabolism on the B vitamins^{20, 25}

Bold arrows indicate the main breakdown route. In vitamin B₆ deficiency, kynureninase is inactivated more strongly than the transaminases, which are involved in the formation of xanthurenic acid²².



Requirements and deficiency symptoms

In adults the minimum requirement of pyridoxine hydrochloride

the protein intake. In infants it is between 0.1 and 0.5 mg per day and is dependent on the protein intake (20 μ g/g protein), the minimum requirement of children is 0.5–1.5 mg per day, that of adolescent 1.5–2 mg per day²⁴. The Food and Nutrition Board (USA) recommend a vitamin B₆ intake of 2.0 mg per day when the daily protein intake is 100 g or more²⁵. The human vitamin B₆ requirement has been the object of much discussion^{21, 22}, it is possible that even higher intakes than those mentioned are needed in

the vitamin B₆

The symptoms of vitamin B₆ deficiency vary greatly with the species and age of the individual. The great variety of deficiency symptoms observed is in part due to the fact that in progressive B₆ deficiency not all the enzyme systems are blocked simultaneously

Enzymatic reactions with pyridoxamine phosphate and pyridoxal phosphate as cofactors*

Enzyme	Reaction	Enzyme	Reaction
Diaminoxidase, histaminase	Oxidation of diamines and histamine	Decarboxylases	For example, decarboxylation of histidine to histamine, tyrosine to tyramine, dopa to dopamine, hydroxytryptophan to serotonin
Serine hydroxymethyl transferase	Formation of 5,10-methylene tetrahydrofolic acid	Threonine aldolase	Breakdown of threonine to glycine and acetaldehyde
α -Glucan phosphorylase	Phosphorolysis of glycogen	Dehydratases	Deamination of serine, homoserine, threonine, etc.
Transaminases	Amino acids + keto acids \rightleftharpoons keto acids + amino acids (with all naturally occurring amino acids)	Desulphhydrases	Deaminating desulphhydration of cysteine and homocysteine
Synthases	Formation of tryptophan from serine and indole, of cysteine from serine, of methionine from serine and methionine	Racemases	L-amino acid \rightleftharpoons D-amino acid (alanine, methionine, glutamic acid)

the same extent²⁷. The following symptoms have been observed in experimental B₆ deficiency³¹: in rats, severe dermatitis (rat pellagra), occasionally haemolytic anaemia and overall loss of body fat; in rabbits, desquamating dermatitis of the ears, mild anaemia, convulsions, creatinuria, paralytic collapse and death³⁵; in rhesus monkeys, arteriosclerosis, dental caries, fatty degeneration or cirrhosis of the liver, pancreatic sclerosis, disturbances of the central nervous system³⁶; in man, (a) skin and mucosa: seborrhoeic and desquamative dermatitis of the mouth and eyes which may spread to the face, scalp, neck and loins; intertrigo of the breasts and inguinal region in women; stomatitis and glossitis; (b) nervous system: irritability, depression, somnolence, nausea, impairment of sensitivity to vibration and positional change; very rarely peripheral neuritis³⁷.

Spontaneous vitamin B₆ deficiency is rare in man. Among 300 infants who received only about 60 µg vitamin B₆ per litre of formula milk (as a result of a new sterilization process) hyperacusis, nervousness and epileptiform convulsions were observed³⁸. Of possible genetic origin are the pyridoxine-dependent convulsions

the following weeks)³⁸⁻⁴⁰; these are probably due to an unsatisfied vitamin B₆ requirement or to a disturbance of vitamin B₆ utilization. Similar causes are probably at the root of the pyridoxine-deficiency anaemia and the pyridoxine-sensitive anaemia seen in man^{38, 41, 42}, but in contrast to the central nervous disturbances these are observed almost solely among adults. In pyridoxine-deficiency anaemia (a hypochromic microcytic anaemia with increased serum iron and organ haemosiderosis) there is a disturbance of δ-aminolaevulinic acid synthesis, with consequent reduction in the amount of protoporphyrin formed; this disease is also probably of genetic origin. In pyridoxine-sensitive anaemia (symptoms as in the deficiency anaemia but often including enlargement of the liver and spleen) there is a complex disturbance of porphyrin metabolism resembling that in siderochrestic anaemia.

It is uncertain whether vitamin B₆ deficiency in man causes dental caries⁴³ or the formation of oxalate stones in the urinary tract⁴⁴.

Cystathionuria is probably due to a defect in the linkage of the coenzyme pyridoxal phosphate to the apoenzyme of homoserine dehydratase (cystathionase)⁴⁵.

Biochemically, vitamin B₆ deficiency is recognizable (a) by the increased excretion of xanthurenic acid and other tryptophan metabolites in urine, especially following oral doses of tryptophan (tryptophan loading test)²⁰; this disturbance of tryptophan metabolism appears after only one week on a vitamin B₆-deficient diet⁴⁶; (b) by a lowered pyridoxal phosphate level in the blood and a greatly reduced vitamin B₆ and pyridoxic acid excretion in the urine⁴⁷; (c) by a reduced transaminase content of the serum⁴⁷ and erythrocytes⁴⁸; (d) by an increased urinary oxalic acid excretion^{44, 49} and a lowered urinary taurine excretion⁴⁹.

Treatment

When the vitamin B₆ deficiency is purely alimentary, daily doses of the vitamin at the level of the normal requirement suffice. In pyridoxine-dependent convulsions in infants pyridoxine should be given parenterally at the rate of 2-15 mg per day⁴⁰; in pyridoxine-deficiency anaemia the dose should be at least 10 mg per day⁴¹ and in pyridoxine-sensitive anaemia at least 500 mg per day⁴¹. Daily pyridoxine supplements of 10-15 mg may be helpful in overcoming disturbances of pregnancy such as severe vomiting and toxæmia, particularly when the diet is poor⁵⁰. Pyridoxine doses of 100 mg have been recommended for the treatment of radiation sickness⁵¹. The success of treatment with pyridoxine is conditional on there being no disturbance of the conversion into pyridoxal (by the action of pyridoxine dehydrogenase) in the body⁶.

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Nicotinic acid¹⁻³ (for references see page 478)

Chemistry

For structure and properties of nicotinic acid and related compounds see the table opposite.

Assay

*Biological*⁴. Black tongue curative test in dogs, growth of chicks.

*Microbiological*⁵. With *Lactobacillus plantarum* (earlier *L. arab*) or *Tetrahymena pyriformis* for nicotinic acid and nicotinamide.

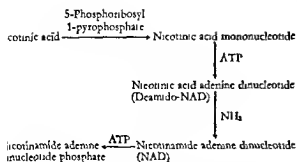
*Chemical*⁶. In pure solution spectrophotometrically, polarographically, by mass analysis, colorimetrically by the bromocresol (KÖNIG) reaction or fluorometrically (the latter method particularly suitable for organs). Nicotinic acid and its metabolites can be separated by chromatographic methods. NAD and NADP are hydrolysed before being determined as nicotinic acid; they are estimated directly by the spectrophotometric or fluorimetric methods through their blue fluorescence in alkaline solution.

Unit

No international unit; by weight.

Biogenesis^{7, 8}

In plants nicotinic acid arises by condensation of 3- and 4-carbon units. In animals, fungi and a few bacteria (for instance, *Xanthomonas pruni*) nicotinic acid is formed from tryptophan by the action of thiamine, riboflavin and vitamin B₆ (see diagram on page 478). It is less likely that nicotinamide is formed directly from nicotinic acid than by the hydrolysis of nicotinamide dinucleotides. The compounds are formed in erythrocytes, liver, yeast, etc. in accordance with the following scheme:



Intake and excretion

In the USA the daily average diet contains about 500–1000 mg of nicotinic acid and 8–17 mg of nicotinamide. Nicotinic acid and nicotinamide are readily absorbed in the intestinal tract. Nicotinic acid is excreted in the urine as nicotinic acid or as its conjugates with glycine (as nicotinuric acid).

Nicotinic acid and nicotinamide raise the dinucleotide content of the erythrocytes. In the form of dinucleotides, nicotinic acid occurs in all tissues, particularly the liver. The human liver contains on the average 65 mg nicotinic acid¹².

In the liver, nicotinamide but not nicotinic acid is methylated to 1-methylnicotinamide with S-adenosylmethionine as methyl donor.





Function

The active forms of nicotinic acid are the nicotinamide dinucleotides NAD and NADP. These are coenzymes (cosubstrates) of

many reactions, particularly those involving the transfer of electrons in reaction with oxygen to form water (oxidative phosphorylation), for details see pages 403–404.

Nicotinic acid but not nicotinamide has an inhibiting effect at high dosage on the synthesis of lipids, particularly cholesterol, but

Uses and properties of nicotinic acid and related compounds

Compound	Formula and mol wt	Structure	Physical properties	Occurrence and activity
Nicotinic acid* (niacin, pyridine-3-carboxylic acid, vitamin PP)	C ₆ H ₅ N ₂ O ₂ 123.11		White crystals, acid taste, moderately soluble in water and ethanol, stable to heat and oxidation M p 234–237 °C	In plant and animal tissues, component of NAD and NADP
Nicotinamide* (nicotinic acid amide, niacinamide, pyridine-3-carboxylamide, vitamin PP)	C ₆ H ₆ N ₂ O 122.13		White crystals, salty taste, soluble in water and ethanol, stable to heat and oxidation M p 128–131 °C	In plant and animal tissues, component of NAD and NADP
1-Methylnicotinamide (N ₁ -methylnicotinamide)	C ₇ H ₈ N ₂ O 137.16			In urine, metabolite of nicotinic acid
1-Methyl-6-pyridine-3-carboxylamide (N ₁ -methyl 2-pyridone-5-carboxylamide)	C ₇ H ₈ N ₂ O ₂ 152.15		White crystals, soluble in water and ethanol M p 212–214 °C	In urine, metabolite of nicotinic acid
Nicotinamide adenine dinucleotide (NAD, reduced form NADH)	See page 344	See page 344	Colourless powder, soluble in water, insoluble in ethanol	In all animal and plant cells, coenzyme of many dehydrogenases
Nicotinamide adenine dinucleotide phosphate (NADP, reduced form NADPH)	See page 344	See page 344	Colourless powder, soluble in water, insoluble in ethanol	In all animal and plant cells, coenzyme of many dehydrogenases

* Trivial names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the International Union of Biochemists [Bull. Assoc. Chem. (Aust.), 107, 1 (1965)]

the mechanism of this effect is obscure¹²; the primary action of nicotinic acid is possibly the liberation of free fatty acids blocked in the tissues¹⁴.

Requirements and deficiency symptoms

The nicotinic acid requirement can also be met by tryptophan, 60 mg of which corresponds to 1 mg nicotinic acid. The requirement of nicotinic acid depends on the caloric intake. The minimum requirement for preventing pellagra is 4.4 mg per 1000 kcal, or 9 mg for adults whose daily caloric intake is below 2000 kcal⁹. For children and adults the Food and Nutrition Board (USA)⁹ recommend a daily intake of 6.6 mg per 1000 kcal; during pregnancy this should be increased by 2 mg per day, during lactation by 7 mg per day (see page 494). The same daily intake of 6.6 mg/1000 kcal for children and adults is recommended by the Joint FAO/WHO Expert Group²² (see page 493); for infants the latter accept that breast feeding by well-nourished mothers will supply adequate niacin equivalents.

Good sources of nicotinic acid are yeast, liver, lean meat, groundnuts and leguminous plants (see pages 499–515). Plant proteins contain 0.8–1.4% tryptophan, animal proteins about 1.3% (see page 516). Maize is low in both nicotinic acid and tryptophan; nicotinic acid is also present in the combined form so that it is not available to the organism¹⁵. During the roasting of coffee considerable amounts of nicotinic acid are formed from trigonelline¹⁶.

Nicotinic acid deficiency causes pellagra, the development of which is favoured by sunlight and heavy physical work. Alimentary nicotinic acid deficiency is common in areas where maize constitutes the principal foodstuff. Pellagra occasionally occurs in chronic alcoholism, cirrhosis of the liver, chronic diarrhoea, diabetes and neoplasias. In the presence of carcinoid tumours up to 60% (normally 1%) of the body's tryptophan is converted into serotonin, so that it is no longer available as a source of nicotinic acid¹⁷. Treatment with isoniazid can cause inhibition of the activity of pyridoxal phosphate and thus interfere with the synthesis of nicotinic acid from tryptophan. This synthesis is possibly also impaired by diets containing large amounts of leucine¹⁸.

The following are the symptoms of pellagra: (a) A dark red erythema appearing symmetrically on the extremities, face, neck and all other regions exposed to air and light; the skin finally becomes dry, fissured, atrophic and brown-coloured. The lesions are marked by atrophy of the superficial layers of the corium with dilatation of the blood vessels, keratinization of the epidermis and a tendency for the latter to separate from the corium. Wounds of any kind exacerbate these symptoms. (b) Chronic inflammation of the mucosa and intestinal tract (stomatitis, glossitis, gastritis with low acid secretion); profuse and often bloody diarrhoea. (c) Emotional disturbances (delirium, hallucinations, confused mental states). Neurological disturbances, if present, are probably due to simultaneous deficiency of other vitamins since these symptoms have not been observed in experimental nicotinic acid deficiency².

The biochemical signs of nicotinic acid deficiency are the following: in pellagra a urinary excretion of 1-methylnicotinamide plus 1-methyl-2-pyridonecarboxylamide of usually less than 2 mg per day. Within 30–60 days the excretion of these metabolites falls to a minimum value and then remains constant; shortly after this minimum value is reached, the first clinical signs of deficiency appear². On a standard diet (10 mg nicotinic acid plus 1000 mg tryptophan) the excretion of nicotinic acid metabolites is less than 3.0 mg in pellagra patients and 7–37 mg in healthy persons¹⁹. In nicotinic acid deficiency the concentration of nicotinamide dinucleotides in the muscles and liver falls, but not that in the erythrocytes^{2,20}.

Treatment

In severe nicotinic acid deficiency, 300–500 mg nicotinamide should be given in daily oral doses of 50–100 mg; if there is difficulty in swallowing, 100 mg nicotinamide should be given three times per day intramuscularly². Nicotinic acid should not be given intravenously in doses exceeding 25 mg owing to the danger of anaphylactic shock. In high doses nicotinic acid but not nicotinamide causes marked dilatation of the vessels and particularly of the capillaries and vessels of the upper half of the body; this is of therapeutic use in disturbances of the peripheral circulation. Nicotinic acid can be used to lower the serum cholesterol level and for this purpose is usually given at the rate of 1 g three times per day²¹.

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Folic acid group^{1–3}

Chemistry⁴

For structure and properties of folic acid and related see the table on pages 480–481.

Assay

Biological. Curative test on chickens⁵.

Microbiological^{1, 6}. With *Lactobacillus casei* (total folic acid: pteroylglutamic acid, pteroyltriglutamic acid and hydrolyses, reduced folic acid including 5-methyltetrahydropteroylglutamic acid); with *Streptococcus faecalis* (pteroylglutamic acid, but not 5-methyltetrahydropteroylglutamic acid); with *Pedococcus cerevisiae* (reduced folic acid). In biologic particularly foodstuffs, the conjugates can also be biogenically.

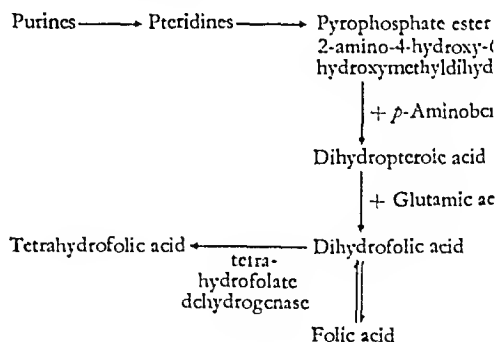
Chemical⁷. Photometrically after fission with zinc or permanganate and subsequent diazotization; in pure substances spectrophotometrically or polarographically.

Units

No international unit; by weight.

Biogenesis⁸

Folic acid is synthesized by higher plants, by microorganisms (intestinal flora) and in animal tissues⁹, probably in accordance with the following scheme:

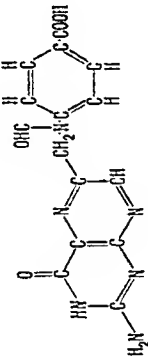
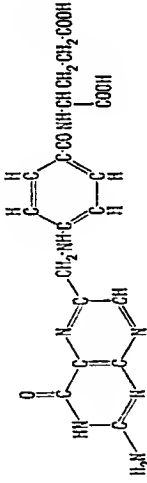
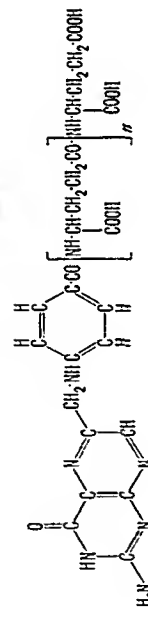
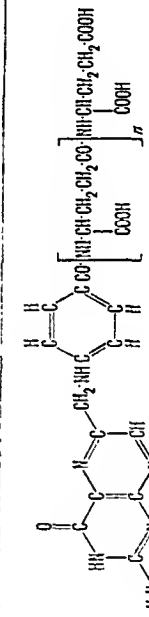
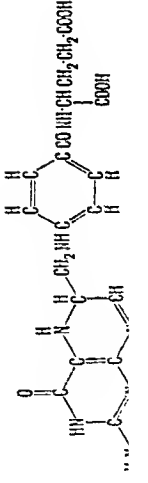



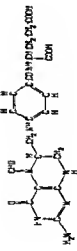
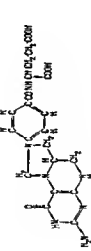
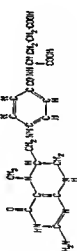
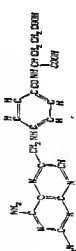
The biosynthesis of dihydrofolic acid is inhibited by amides¹⁰. Folic acid antagonists like aminopterin and its derivatives with a structure resembling pyrimidine (e.g., primidone, methaminc) inhibit tetrahydrofolate dehydrogenase and the formation of tetrahydrofolic acid.

Intake and excretion

In USA the daily diet contains about 150–200 µg activity^{11, 12}; this includes only about 20 µg pteroylglutamic acid.

Structure and properties of folic acid and related compounds

Names*	Formula and mol. wt.	Structure	Physical properties	Occurrence and biological properties
Rhizopterin (SLR factor)	$C_{13}H_{12}N_6O_4$ 340.30		Light-yellow platelets	In fermentation juice of <i>Rhizopus migrans</i> . Weak folic acid activity
Pteroylglutamic acid (folic acid, folacin, vitamin B ₉ , p-[2-amino-4-oxo-5-hydroxy-6-methylaminobenzoyl]-L-glutamic acid)	$C_{19}H_{18}N_7O_8$ 441.41		Orange-yellow needles or platelets, odourless and tasteless [α] + 20° in 0.1-N NaOH	In liver, yeast, green leaves. Growth factor for <i>Lactobacillus casei</i> , <i>Streptococcus faecalis</i> R and other micro-organisms. Anti-anæmic properties
Pteroyltriglutamic acid, PteGlu ₃ (teropterin)	$C_{29}H_{24}N_{10}O_{12}$ 699.64		Light-yellow amorphous powder $n = 2$	In micro-organisms; formed in fermentations induced by corynebacterin. Weak folic acid activity
Pteroylheptaglutamic acid, PteGlu ₇ (vitamin B ₉ conjugate)	$C_{49}H_{40}N_{14}O_{24}$ 1216.11		Orange crystals $n = 6$	In yeast. Microbiologically inactive; presumably the form in which pteroylglutamic acid is stored
Dihydropteroylglutamic acid, H ₂ PteGlu (dihydrofolic acid, DHF)	$C_{19}H_{18}N_7O_8$ 443.42		Light-yellow amorphous powder	Intermediary metabolite

amic acid, H_4PteGlu (tetrahydrofolic acid, THF)	445 44			powder, exothermic in air, unstable to light, partic- ularly in solution (-)- α -Form: $[\alpha]_D^{25} -16.9^\circ$	
5-Formyltetrahydro- pteroylglutamic acid (leucovorin factor, folic acid, leuco- vorin)	$\text{C}_{19}\text{H}_{24}\text{N}_8\text{O}_6$ 473 45			Colorless crystals $[\alpha]_D^{20} -15.1^\circ$ (natural factor) $[\alpha]_D^{25} +16.76^\circ$ (racemate, synthetic factor)	In micro-organisms. Growth fac- tor for <i>Leuconostoc citrovorum</i> , <i>Lacto-</i> <i>bacillus lactis</i> , <i>Streptococcus faecalis</i> , <i>Lactobacillus acidophilus</i> , carrier of one-carbon units
5,10-Methylenetetra- hydropteroylglutamic acid (active formaldehyde)	$\text{C}_{20}\text{H}_{26}\text{N}_8\text{O}_6$ 457 45			Usable in acid and neutral media	Carrier of one-carbon units
5-Methyltetrahydro- pteroylglutamic acid	$\text{C}_{21}\text{H}_{28}\text{N}_8\text{O}_6$ 459 47				In serum and liver. Carrier of one- carbon units
4-Aminopteroylglutamic acid (aminopterin)	$\text{C}_{21}\text{H}_{26}\text{N}_8\text{O}_6$ 440 42			Yellow needles	Antagonist of folic acid, inhibits cell division

* In accordance with the recommendations of the Commission on Biochemical Nomenclature of the IUPAC (IUPAC-NUB Commission on Biochemical Nomenclature [*Biochimie* *hypoth. Acta* (*Ann.*), 107, 11 (1963)] the names "folic acid" and "folate" should be used only as general designations for compounds of the group or mixtures of such compounds and not for any compound named on the basis of its structural formula.

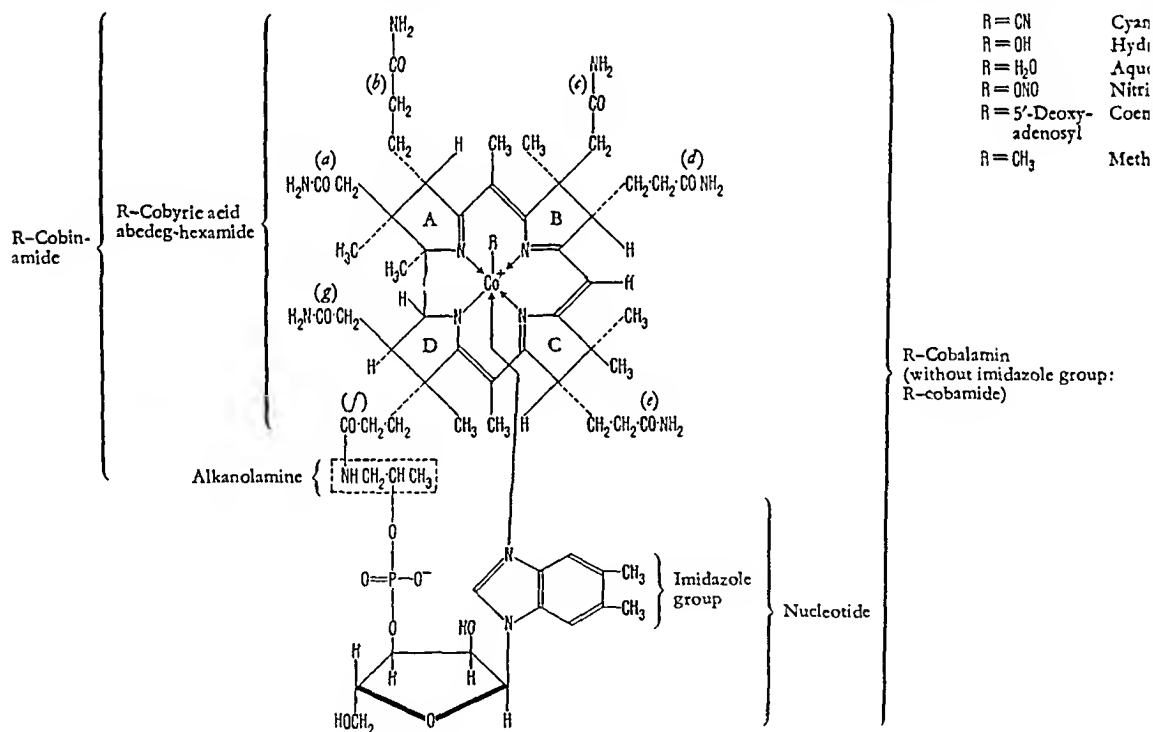
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Vitamin B₁₂ group (corrinoids)^{1,2} (for references see page 485)

Chemistry³

All the complete B₁₂ vitamins contain an α -glycosidic nucleotide. The imidazole nitrogen atom of this nucleotide can become co-ordinated under suitable conditions with the cobalt atom. In the case of the incomplete types either the alkanolamine and nucleotide

portion, or simply the latter, is lacking; in some cases the portion is β -glycosidic, when the imidazole nitrogen become co-ordinated with the cobalt atom. The B₁₂ co respond to the complete B₁₂ types but in place of the im they possess an organic group linked directly via a ca the cobalt atom. The complete and incomplete B₁₂ type to light and oxygen are presumably artefacts of the B₁



Names*	Formula and mol. wt.	Physical properties	Occurrence and biological properties
Complete B₁₂ types			
Vitamin B ₁₂ (cyanocobalamin, 5,6-dimethylbenzimid- azolylcyanocobamide)	C ₆₃ H ₈₈ N ₁₄ O ₁₄ PCo 1355.40	Red needles, stable on heating several hours at 100 °C. Spectral absorption in water: maxima at 278, 361, 550 nm	Occurs in nature as coenzyme. Ca lated from animal tissues, many s bacteria, sewage sludge, activated Stimulates maturation of erythr bone marrow; acts as animal prot in animals; promotes growth o micro-organisms
* Trivial names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and national Union of Biochemistry [<i>Biochim. biophys. Acta (Amst.)</i> , 117, 285 (1966)].			

Names*	Formula and mol wt.	Physical properties	Occurrence and biological properties
cobalamin min B ₁₂ , (methylbenzimid- ylaquocobamide) cobalamin min B _{12a} , (methylbenzimid- ylhydroxocob- amide)	C ₆₃ H ₉₈ N ₁₄ O ₁₄ PCo 1347.39	Red needles, aquo form in neu- tral solution, hydroxo form in alkaline solution Spectral absorption in water: maxima at 274, 350, 522 nm	Activity as for cyanocobalamin, depot form in the human body
5-lybenzimidazolyl- cobamide		Red needles	In sewage sludge and activated sludge. Rep- resents two-thirds of the cyanocobalamin activity in pernicious anaemia
5-ridazolylcyanoco- bide		Red needles	In sewage sludge and activated sludge. Rep- resents two-thirds of the cyanocobalamin activity in pernicious anaemia
5-oxylbenzimidazolyl- cobamide (tor III)		Red needles	Inactivated sludge, weakly active in perni- cious anaemia
5-vitamin B ₁₂ nuncyanocob- amide)		Red needles	Inactivated sludge, faeces, stomach con- tents of ruminants; inactive in pernicious anaemia
5-yladeninecyanocob- amide (tor A)		Red needles	Inactivated sludge, faeces, stomach con- tents of ruminants; very weakly active in pernicious anaemia
<i>Incomplete B₁₂ types</i>			
5-cobalamin tor B, cyanocob- amide)		Amorphous	Inactivated sludge, faeces, stomach con- tents of ruminants; antagonist of cyanoco- balamin in the chick test
<i>B₁₂ coenzyme</i>			
5-adenosylcobal- min (coenzyme B ₁₂)		Orange-yellow platelets, photosensitive	In many species of bacteria, in animal tissues (mainly liver). Biochemically active form of vitamin B ₁₂ . Growth promoting activity for micro-organisms and chicks; activity in pernicious anaemia as for cyanocobalamin, depot action in the human body
5-cobalamin		Orange-yellow platelets, photosensitive	In animal tissues (liver), blood serum. Coenzyme function

* Names recommended by the Commission on Biochemical Nomenclature of the International Union of Pure and Applied Chemistry and the Inter-
national Union of Biochemistry [Biochim Biophys Acta (Amst), 117, 285 (1966)]

biological: * With bacteria: *Escherichia coli* (cobalamin, cob-
pseudo-vitamin B₁₂), *Lactobacillus leichmanni* (cobalamin,
vitamin B₁₂). With protozoa: *Evelina granitii* (cobalamin,
vitamin B₁₂), *Ochromonas malhamensis* (cobalamin only).
† *in vitro* Spectrophotometrically or polarographically in pure
solution, separation of the individual compounds by counter-
diffusion, column chromatography or ion exchange
chromatography. ‡ Tagging of vitamin B₁₂ with ⁵⁷Co, ⁶⁰Co

Unit

No international unit, by weight: 1 µg vitamin B₁₂ = 11000 I.U.
(*Lactobacillus lactis* Dorsey). Units = 1 USP Unit (live)
1 USP Unit is the daily dose that produces a clinically and
logically satisfactory response in true pernicious anaemia. †
standpoint of activity, 1000 I.U. Units corresponds to
1 ml of a good liver extract

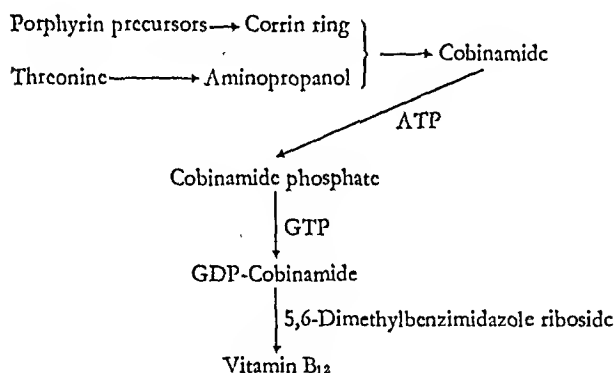
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* Reference Preparation see page

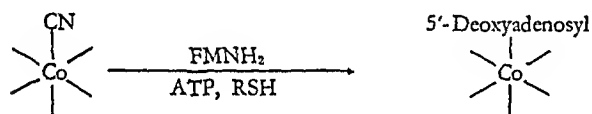
Biogenesis^{6,7}

Vitamin B₁₂ is synthesized by many species of bacteria, in particular the propionibacteria and *Aerobacter aerogenes*. It is possibly also formed in animal tissues⁸.

The biosynthesis is in accordance roughly with the following scheme:



This process results in formation of the coenzyme forms of the vitamin; cyanocobalamin and hydroxocobalamin are probably only artefacts⁹; they can, however, be converted in animal tissues into the coenzymes:

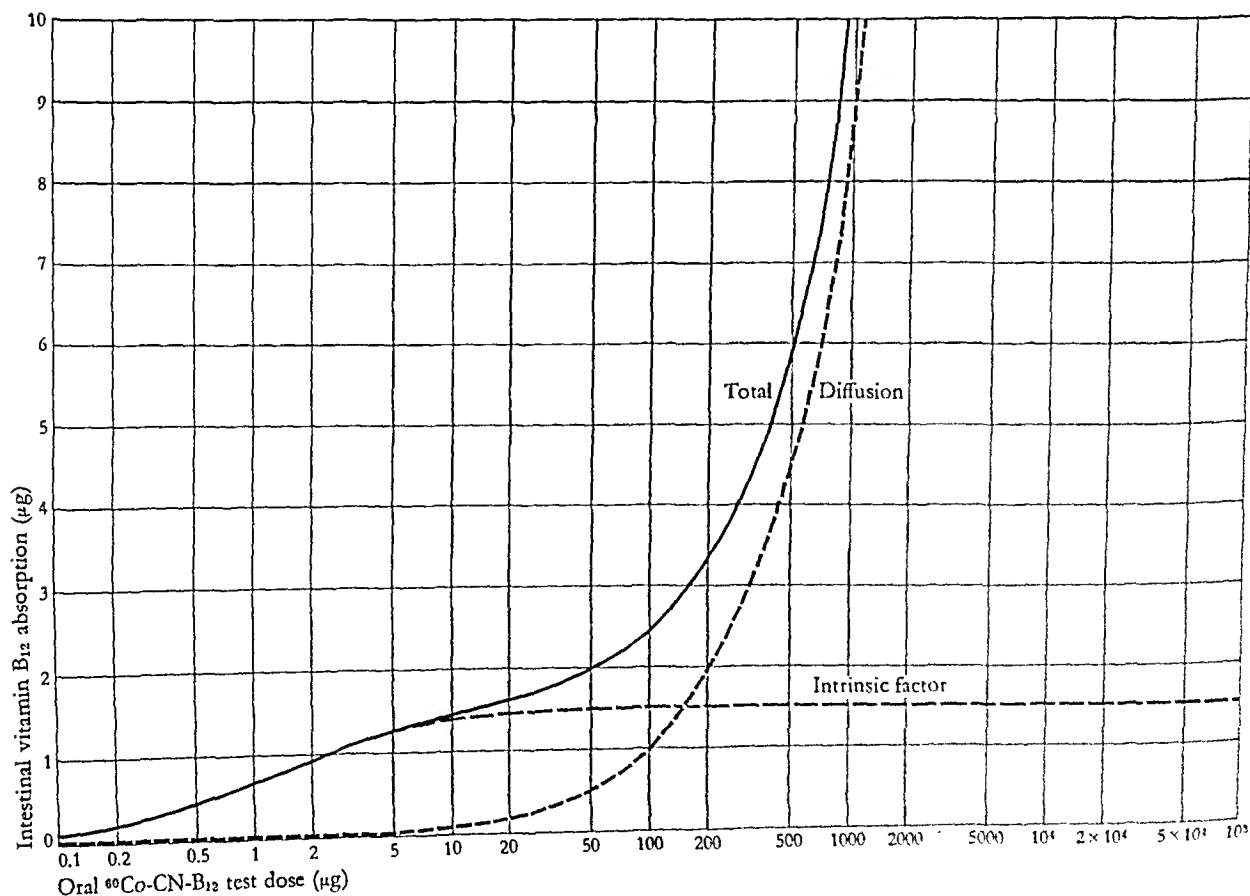


Intake and excretion

In the USA the average daily diet contains 15–30 µg vitamin B₁₂¹⁰, of which perhaps 5 µg is absorbed. According to HEINRICH and WOLFSTELLER¹², of any dose of vitamin B₁₂, 1.5 µg is absorbed in the ileum with the aid of the so-called *intrinsic factor*, a mucoprotein of the gastric juice¹¹; transport through the intestinal wall probably takes place together with the intrinsic factor¹³. In addition, there is passive diffusion through the intestinal wall¹⁴ to an extent that increases logarithmically with increasing size of the dose up to a limiting value of 0.9% of the dose¹². On a normal diet and three meals a day this means that 2–5 µg or more of vitamin B₁₂ is absorbed daily¹⁵ (see the figure below). Cyanocobalamin is rather more easily absorbed than coenzyme B₁₂¹⁶. Some 10–15 µg vitamin B₁₂ is synthesized daily by bacteria in the human large intestine, and about the same quantity is excreted daily in the faeces; whether any of the quantity formed by bacterial synthesis is absorbed is doubtful¹⁷.

The vitamin B₁₂ content of the serum lies in the range 100–900 ng/l (see page 610); here the vitamin is mainly present as methylcobalamin, about 80% being bound to α-globulins (transcobalamin I). Exogenous vitamin B₁₂ becomes bound for a short time to β-globulin (transcobalamin II)¹⁸. The half-life of intravenously administered cyanocobalamin in the serum is about 6 days¹⁹. Small doses of a few microgrammes of vitamin B₁₂ are retained in the body but doses of a few milligrammes are rapidly excreted in the urine. Hydroxocobalamin given parenterally is retained in the body longer than cyanocobalamin or coenzyme B₁₂¹⁶. In the tissues the vitamin is probably stored as the coenzyme. The total body stores of the vitamin have been estimated at 2–5 mg (range 1–11 mg)^{1,12,15}. The liver contains about 0.8 mg vitamin B₁₂²⁰ (the biological half-life of the vitamin in the liver is about 12 months¹⁹). 0.1% of the body's stores of vitamin B₁₂ is excreted daily¹⁵. These stores probably suffice to prevent the appearance of clinical deficiency symptoms for 3–8 years^{1,15}. Excretion of the vitamin is almost solely in the bile (see page 655), only very small amounts being found in the urine (0–0.27 µg per day)¹. On SCHILLING's excretion test see pages 289 and 485.

Distribution of the total intestinal vitamin B₁₂ absorption in healthy persons between absorption dependent on the intrinsic factor and absorption dependent on diffusion¹²



Biotin'**Chemistry**

For structure and properties of biotin and related compounds see the table below.

Assay

*Biological*³. With *Saccharomyces cerevisiae*, *Lactobacillus casei*, *Lactobacillus arabinosus*, *Neurospora crassa*, etc.; in biological fluids preferably with *Ochromonas danica*.

Chemical. No methods in common use.

Unit

No international unit; by weight. 1 avidine unit = the smallest quantity that completely suppresses the growth-promoting effect in yeast of 1 µg biotin⁴.

Biogenesis^{2, 5}

Biotin is synthesized in plants (particularly in sprouting seeds) and various micro-organisms. Thus *Achromobacter* forms biotin from pimelyl-coenzyme A, cysteine and carbamyl phosphate; pimelyl-coenzyme A is formed from 3 molecules of malonyl-coenzyme A⁶.

The carboxyl group of biotin is covalent and bound to the lysine residue of a protein. Biocytin is formed by the action of a proteinase on protein-bound biotin.

Intake and excretion

Biotin is formed by the intestinal flora in such large quantities that it is excreted in the faeces in an amount 2-5 times greater than the dietary intake⁷. The body appears to be capable of utilizing biotin formed in the intestine but to an unknown extent. The avidine present in raw egg-albumin combines with biotin, thus rendering it useless for the organism.

Biotin has been detected in whole blood and serum (see page 611) and in urine (see page 676). Small quantities are stored in the liver (about 0.2 mg) and in the brain^{3, 8} (blood vessels 3-5 ng/g⁹). In the liver, biotin is mostly bound to protein (in rats 90%⁸). Little is known of the metabolism of biotin. In rats given injections of biotin 16% was found 4 hours later in the liver and 30% was excreted⁸.

Function⁵

Biotin is essential for warm-blooded animals and some micro-organisms. It acts as coenzyme in CO₂-fixation and transcarboxylation reactions.

Structure and properties of biotin and related compounds

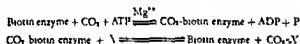
Names	Formula and mol. wt.	Structure	Physical properties	Occurrence	Activity
Biotin, <i>d</i> -biotin	C ₁₀ H ₁₆ N ₂ O ₃ S 244.31		White needles, stable to heat, unstable to acids and alkalis M.p. 230-232 °C [α] _D ²⁰ +91° in 0.1-N NaOH	Various micro-organisms, for example yeasts, animal tissues, particularly liver, egg-yolk, plants	Growth factor for many bacteria, protozoa and probably all higher animals
Biocytin, <i>d</i> -biocytin (ε- <i>N</i> -biotinyl-L-lysine)	C ₁₆ H ₂₆ N ₄ O ₄ S 372.49		M.p. 245-252 °C	Yeasts	Growth factor for various micro-organisms
Biotin sulphoxide, <i>d</i> -biotin 1-sulphoxide (AN factor)	C ₁₀ H ₁₆ N ₂ O ₄ S 260.31			Cultures of <i>Aspergillus niger</i> and <i>Phycomyces blakesleeana</i>	Growth factor for <i>Neurospora crassa</i>
Oxybiotin (oxobiotin)	C ₁₀ H ₁₆ N ₂ O ₄ 228.25		M.p. 205-207 °C		5-30% of activity of biotin ²
1'- <i>N</i> -Carboxybiotin (CO ₂ -biotin)	C ₁₁ H ₁₆ N ₂ O ₅ S 288.33			Unstable intermediate	Active form of CO ₂ in carboxylations

Biotin – Panto

Biotin enzymes

Enzyme	Reaction catalysed	Occurrence
Acetyl-CoA-carboxylase	acetyl-CoA + HCO_3^- + ATP \rightleftharpoons malonyl-CoA + ADP + P	Micro-organisms, chicken liver
β -Methylcrotonyl CoA-carboxylase	β -methylcrotonyl-CoA + HCO_3^- + ATP \rightleftharpoons β -methylglutaconyl-CoA + ADP + P	Micro-organisms, rat liver mitochondria
Propionyl-CoA-carboxylase	propionyl CoA + HCO_3^- + ATP \rightleftharpoons methylmalonyl-CoA + ADP + P	Swine heart, ox liver mitochondria
Methylmalonyl-CoA-carboxyl-transferase	methylmalonyl-CoA + pyruvate \rightleftharpoons propionyl-CoA + oxalacetate	Propionibacteria, skeletal muscle of dogs
Pyruvate carboxylase	pyruvate + HCO_3^- + ATP \rightleftharpoons oxalacetate + ADP + P	Micro-organisms, liver mitochondria, rabbit kidneys

The carboxylation reactions catalysed by the biotin enzymes have the general form



an important role in many other reactions in which, however, it acts only in an indirect manner. Examples of such reactions are the deamination of aspartate, serine and threonine in bacteria, deamination of serine in animals, reductive carboxylation of pyruvate, carboxylation of phosphoenol pyruvate, carbamylation reactions, tryptophan metabolism, purine synthesis, protein synthesis and carbohydrate metabolism.

Certain biotin homologues (homo-oxybiotin, biotinsulphone, in which the sulphur atom is replaced by a sulphone group) act as anti-vitamins¹².

Requirements and deficiency symptoms

The biotin requirement of man is unknown. In experimental biotin deficiency, doses of 150–300 μg per day sufficed to suppress the deficiency symptoms^{13, 14}; this amount is provided by a normal diet¹⁵.

Substances rich in biotin are liver, kidneys, yeast and egg-yolk; the vitamin is also present in vegetables, nuts and cereals (see pages 498–515).

Biotin deficiency is manifested¹⁶ in nervous disturbances (rats, pigs, chickens, man), hyperkeratosis (rats), seborrhoeic dermatitis (man), loss of hair (rats, mice), loss of hair pigment (rats, mice). Experimental biotin deficiency in man results in lethargy, loss of appetite, nausea, muscular pain and localized paraesthesia¹⁷. Spontaneous biotin deficiency has been reported following a diet rich in raw eggs^{18, 19} and also appears to be associated with liver cirrhosis¹⁶.

Treatment

Biotin has been used to treat seborrhoeic dermatitis in young children (Larssen's disease)²⁰, which is possibly due to a deficiency of biotin in the breast milk together with loss of the vitamin due to persistent diarrhoea.

Structure and properties of pantothenic acid and related compounds

Compound	Formula and mol. wt.	Structure	Physical properties	Occurrence and activity
Pantothenic acid (D-[+]-N-[α , γ -dihydroxy- β -dimethylbutyryl]- β -alanine, chick antidermatitis factor)	$C_9H_{17}NO_5$ 219.24		Yellow oil, unstable to heat, acids and alkalis [α] _D ²⁵ + 37.5° Calcium salt: white crystals, stable to heat	Widely distributed in plants and animals. Growth factor for yeast, many other micro-organisms and all high animals; component of coenzyme A
Pantothenyl alcohol (panthenol, N-pantoyl-3-propanolamine)	$C_9H_{19}NO_4$ 205.26		Viscous liquid [α] _D ²⁵ + 29.5°	Synthetic. Shows 86% of activity of pantothenic acid in the chick test ²
Pantethein (N-pantotheryl- β -aminoethanethiol)	$C_{11}H_{22}N_2O_4S$ 278.37		Amorphous powder soluble in water	Growth factor for <i>Lactobacillus bulgaricus</i>
Coenzyme A (CoA)	$C_{21}H_{38}N_7O_{16}P_3S$ 767.54	See page 345	Colourless powder soluble in water	Widely distributed in micro-organisms, plants and animals. See also text and page 345

intestine, though it is not known whether the body makes use of this source. The pantothenic acid content of whole blood is ca. 0.2–2 mg/l (see page 611), that of the spinal fluid about the same (see page 639). Urinary excretion of the vitamin amounts to 0.76–4.1 mg/l⁹ (see also page 676). Four hours after giving a test dose of the vitamin there is a sharp rise in the blood and urine levels⁹. In blood and spinal fluid pantothenic acid is in the conjugated form, whereas in the urine it is in the free form⁹. The excretion in the faeces is very variable and depends on the nature of the diet.

Coenzyme A is not present in the circulating blood and appears to pass the cell membrane only with difficulty. It is probably formed within the cell when required. Coenzyme A occurs mainly in the following organs (in order of decreasing concentration): liver, adrenals, kidneys, brain, heart, testes. The pantothenic acid content of the human liver amounts to 28 mg, mainly as coenzyme A⁹.

Function

The importance of pantothenic acid in metabolism is explained by its presence in coenzyme A. In the form of acetyl-coenzyme A ('active acetic acid') it is responsible for transport of two-carbon and other acyl groups (see page 345). Coenzyme A is involved in the following reactions: formation of citrate from oxalacetate and acetate (pages 390 and 424), oxidation of pyruvate (page 391), oxidation of α -ketoglutarate (page 390), oxidation and synthesis of fatty acids (pages 391 and 424), synthesis of triglycerides (page 426), phospholipids (page 425) and cholesterol (page 426), acetylation of amines (page 444), choline (page 434) and glucosamine (see page 424). Pantothenic acid plays an important part in the activity of the adrenal cortex¹⁰ since the corticosteroids are formed from the cholesterol synthesized with the participation of coenzyme A (page 429).

Requirements and deficiency symptoms

The human pantothenic acid requirement is unknown, but children and adults it is probably met by an intake of 5–10 mg/day¹¹, an amount normally present in the diet. The requirements of children are lower in accordance with their smaller intake of calories¹².

Pantothenic acid is present in almost all vegetables, cereals and animal foods. Good sources of the vitamin are yeast, liver, kidney, heart (see pages 499–515) and particularly the jelly queen bees feed on (royal jelly), containing 110–320 μ g/g¹³.

Pantothenic acid is so widely distributed in foods that deficiency is practically unknown in man. Deficiency symptoms in animals are degeneration of the neuromuscular structures and adrenal insufficiency, and death may ensue. An experimental deficiency has been produced in man by means of a diet low in the vitamin together with doses of the antagonist Ω -methylpantothenic acid¹⁴, with the following symptoms: mild fatigue, headache, sleeplessness, nausea, epigastric pain, paraesthesia of the limbs, muscle spasms and coordination disturbances; other signs were absence of the cosine phase reaction of the blood to ACTH and an increased sensitivity to insulin. The pantothenic acid deficiency was evidenced by the reduced acetylating capacity of the blood after administration of sulphamylamide or para-aminobenzoic acid.

Treatment

The so-called 'burning feet' syndrome has been treated with pantothenic acid¹⁵, though it is not certain that this is solely due to pantothenic acid deficiency. Pantothenic acid has also been reported to be effective against the neurotoxic effects of strychnine; its value in the treatment of emotional disturbances, neurasthenia, neuropathy¹⁷, skin diseases¹⁷ and paralytic ileus¹⁸ is

ascorbic acid¹⁻³ (for references see page 491)

chemistry

Compound	Formula and mol wt	Structure	Physical properties	Occurrence and activity
L-Ascorbic acid (vitamin C)	$C_6H_8O_6$ 176.13		White crystals with an acid taste, soluble in water, rather insoluble in ethanol, sensitive to light, atmospheric oxygen and some heavy metals, strong reducing action M p. 192 °C, $[\alpha]_D + 23^\circ$	Probably present in all higher plants, particularly cabbage, citrus fruits, hawthorn berries, in small amounts in animal tissues. Antiscorbutic activity
Dehydroascorbic acid	$C_6H_6O_6$ 174.11		White crystals, soluble in water, readily hydrolysed to 2,3-diketo-L-gulonic acid M p. 225 °C	Present with ascorbic acid in plants. Antiscorbutic activity
2-Keto-L-gulonic acid	$C_6H_{10}O_7$ 194.14		White crystals M p. 171 °C	Precursor of ascorbic acid. No antiscorbutic activity

Assay

*Biological*⁴ In guinea pigs either by histological study of tooth

(there is some doubt as to whether these are valid for plants)⁴



eye 250, adrenals 400, pancreas 150, liver 150, kidneys 50, heart muscle 50. Tissue levels of ascorbic acid are highest at birth and greatly reduced in old age¹². The saturation level in leucocytes is 270–300 mg ascorbic acid per kg¹¹; high doses of ascorbic acid have been reported to increase this concentration up to 600 mg per kg¹². The whole blood and plasma levels (see page 611) depend on the degree of tissue saturation and on the dietary intake. High doses of ascorbic acid cause the plasma level to rise rapidly, possibly to 40 mg per litre; the normal plasma level is below 14 mg per litre, since at this concentration the threshold value for the kidneys is reached with a consequent steep rise in the ascorbic acid clearance^{3,11}. In the plasma about 20% of the total ascorbic acid is in the form of dehydroascorbic acid¹⁴ (page 611). Ascorbic acid also occurs in the aqueous humour of the eye (50–295 mg/l¹⁵), in gastric juice (see page 650) and in the synovial fluid (see page 642).

Dependence of ascorbic acid levels in serum and leucocytes on intake^{2,3,11}

Daily intake (mg)	Serum (mg/l)	Leucocytes (mg/kg)	Tissue saturation (%)	Percentage of a test dose in the urine*
<10	<2	<120	0–40	<5
10–20	~2	~120	~40	<15
30–100	4–10	150–200	>50	20–60
>100	10–14	270–300	→100	60–80

* The usual loading tests consist either of giving 10 mg ascorbic acid orally per kg body weight followed by determination of ascorbic acid in the 24-hour urine, or of giving 100 mg ascorbic acid intravenously followed by determination of ascorbic acid in the 3-hour urine.

With an ascorbic acid concentration of 20 mg per kg body weight the daily turnover is about 1 mg per kg, corresponding to a half-life of 16 days¹⁶. In urine ascorbic acid appears mainly unchanged (see page 676), but part is hydrolysed to diketogulonic acid and appears finally as oxalic acid³. Other metabolites are L-xylonic and L-lyxonic acids, which arise by decarboxylation of ascorbic acid¹⁷. Radioactive CO₂ has been detected in expired air after giving doses of tagged ascorbic acid¹⁸. The ascorbic acid content of breast milk (page 689) depends largely on the dietary intake.

Function

Ascorbic acid and dehydroascorbic acid form a redox system with 'semidehydroascorbic acid' as highly reactive intermediate. The latter arises by the loss of a single electron by ascorbic acid or by the acceptance of a single electron by dehydroascorbic acid¹⁹. Almost all metabolic processes the disturbance of which gives rise to scurvy involve reactions in which ascorbic acid is oxidized. Of particular importance are the hydroxylation reactions dependent on ascorbic acid which require molecular oxygen.

The disturbances in the formation of connective tissue that appear in ascorbic acid deficiency are a result of failure of the ascorbic acid-dependent hydroxylation of proline to hydroxyproline, a component of collagen. The formation and maintenance of collagen is dependent on a normal ascorbic acid level¹⁹. Synthesis of collagen in human skin-tissue cultures is promoted by ascorbic acid²⁰. In guinea-pigs with ascorbic acid deficiency the formation of hydroxyproline in granulation tissue commences only after ascorbic acid has been administered²¹.

Another hydroxylation reaction dependent on ascorbic acid is the hydroxylation of the side chain of dopamine to noradrenaline; the enzyme catalysing this reaction has been found in the microsomes of beef adrenal cortex²². Ascorbic acid is probably involved also in the hydroxylations occurring in steroid synthesis in the adrenals, but little is known of this role^{22,23}.

Ascorbic acid is also concerned in tyrosine metabolism as reducing agent, although here it does not participate in a hydroxylation reaction. Its probable effect is that of protecting the enzyme para-hydroxyphenylpyruvic acid hydroxylase from inhibition by its substrate²⁴. Ascorbic acid also plays a role as electron donor in the conversion of folic acid into tetrahydrofolic acid. This connection between ascorbic acid and tetrahydrofolic acid may be responsible for the appearance of macrocytic anaemia in scurvy¹⁰. The hypochromic anaemia of scurvy, on the other hand, is more likely to be due to an effect of ascorbic acid on iron metabolism, since the vitamin is necessary for the incorporation of iron into ferritin²⁵.

In contrast to the reactions dependent on ascorbic acid hydroxylation of tryptophan to 5-hydroxytryptophan, the precursor of serotonin, is mediated by dehydroascorbic acid, with thereby reduced to ascorbic acid. The enzyme catalysing this reaction is dependent on copper ions for its activity and occurs in the tissues of the small intestine²⁶. The regeneration of ascorbic acid from dehydroascorbic acid in the tissues plays an important metabolic role. It takes place with the formation of semidehydroascorbic acid from ascorbic acid and dehydroascorbic acid, with an enzyme system present in the animal cell transfers electrons from NADH₂ to semidehydroascorbic acid and so regenerates ascorbic acid¹⁰.

In the animal organism ascorbic acid seems to have a protective action against deficiencies of other vitamins (thiamine, riboflavin, pantothenic acid, biotin, folic acid, vitamin E, vitamin A) relationships between these vitamins and ascorbic acid are, however, obscure²⁷.

Requirements and deficiency symptoms

The minimum intake of ascorbic acid required to prevent scurvy in infants is about 10 mg per day, in adults a little under 10 mg per day²⁸. A daily intake of 30–40 mg results in moderate saturation of the tissues, one of 60–100 mg in almost complete saturation²⁸. recommended daily intakes of ascorbic acid in various countries are as follows: England²²: infants 15 mg, children 20–30 mg, adults 30 mg; USA²⁹: infants 35 mg, children 40–80 mg, adults 60 mg; Western Germany³⁰: infants 30–35 mg, children 40–50 mg, adults 75 mg; Canada³¹: children 20–30 mg, adults 30 mg; Japan³²: children 35–75 mg, adults 50 mg; Japan³³: children 30 mg, adults 60–65 mg. For the recommendations of the Food Nutrition Board (USA)²⁹ for pregnant and lactating women see the table on page 494. Workers in very cold climates should have an intake of 150–250 mg per day³⁴.

Good sources of ascorbic acid are cabbage, spinach, paprika, citrus fruits, tomatoes, strawberries, red currants and liver (pages 499–515). In vegetables the ascorbic acid falls rapidly during withering. Potatoes are an important source of ascorbic acid; the concentration decreases by up to 80% in winter storage. F cow's milk contains up to 25 mg per litre; this is markedly reduced by pasteurization or boiling.

The most important symptoms of ascorbic acid deficiency are a marked tendency to bleeding with the appearance of extensive patches of haemorrhage under the skin and in the gums, muscle fatty tissues and internal organs. Other symptoms are impairment of connective tissue formation with changes in bone structure, growth, defective tooth formation and fissuring and roughening of the skin; there are also often disturbances of iron absorption, anaemia. In infants ascorbic acid deficiency (MOELLER-BARI disease) is manifested mainly in the bones, which show a zone of destroyed bone extending over the margin of the metaphysis into the soft tissues, as well as by subperiosteal bleeding, particularly in the metaphyseal zones of the long bones.

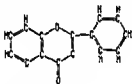


On a diet free of ascorbic acid the ascorbic acid content of plasma falls after 40 days to less than 1 mg per litre, while after 120 days that of the leucocytes is almost zero². At this time there is also enlargement and keratosis of the hair follicles, which in succeeding 40 days gradually develop haemorrhages and the characteristic signs of scurvy; changes in the gingiva appear after 40 days³⁶.

An inadequate intake of ascorbic acid is best recognized by a lowered plasma level, whereas a severe deficiency of the vitamin is characterized by the low ascorbic acid concentration of the leucocytes (<120 mg/kg; see the table above). Various tests are available for measuring the extent to which ascorbic acid is provided in the diet; they depend on the degree of tissue saturation effected by a test dose of the vitamin as indicated by the plasma level and urinary excretion.

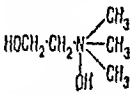
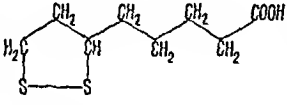
Treatment

In infants, doses of 20 mg ascorbic acid per day, for instance in the form of orange juice, are ample to prevent the appearance of scurvy; in infants with scurvy 25 mg should be given 4 times a day; in adults with the disease 100 mg 5 or 6 times a day²⁸. In patients who have undergone extensive surgery 150–300 mg ascorbic acid per day is sufficient to produce adequate saturation of the tissues. The reducing properties of ascorbic acid can be utilized in the treatment of methaemoglobinemia and to promote the absorption of orally administered iron³⁵. Russian workers have reported success in the treatment of coronary diseases with ascorbic acid³⁶.

Substances with vitamin-like action (vitaminoids)*

Compound	Formula, mol wt and physical properties	Occurrence	Function	Requirements and deficiency symptoms
Bioflavonoids ² (vitamin P group, ettrin)	<p>Structure of the flavones:</p>  <p>Substances like hesperidine and eriodictiol also belong to this group</p>	Widely distributed in plants, particularly in fruits (e.g., lemons and black currants)	Biological function obscure. Views on pharmacological activity vary. Substances increasing capillary resistance probably possess antihistamine and antithyroidase activity ³	
Inositol ² (myoinositol)	 <p>Cell: $C_6H_{12}O_6$ Mol wt 180.16 M p 225-227 °C</p>	Probable component of all living cells. Component of phospholipids in leaves, seeds and animal tissues (particularly heart, brain and skeletal muscle), present as hexaphosphate (phytic acid) in plants	In the phospholipid form involved in cation transport through the cell membranes, in stimulation of nerves and in metabolism of the mitochondria ⁴	Growth factor for yeast and many kinds of animal cells in tissue culture. Synthesized in the animal organism. Significance in human nutrition obscure. Intake about 1 g per day
L-carnitine ² (3-hydroxy-γ-butyrobetaine, vitamin B ₁₂)	 <p>Cell: $C_{11}H_{19}NO_7$ Mol wt 315.30 [α]_D -20.9°</p>	In all animal tissues (skeletal muscle 1, heart 0.6, kidneys 0.4, liver 0.3 mg/gramme dry substance), small amounts in blood, milk, plants and micro-organisms	Involved in intracellular fat metabolism in the form of acylcarnitines by (a) transporting acetyl-coenzyme A and acetoacetyl-coenzyme A from the mitochondria to the site of synthesis of long-chain fatty acids outside the mitochondria; (b) transporting activated long-chain acyl groups from the cytoplasm to the mitochondria, where long-chain fatty acids are oxidized ⁵	Growth factor for some insects, for instance mealworm, <i>Tenebrio molitor</i> and some bacterial species. Vertebrates can synthesize carnitine

* According to Krumm¹ these are substances that must be regarded as essential dietary components for many living organisms but that do not function in the form of enzymes.

Compound	Formula, mol. wt. and physical properties	Occurrence	Fun
Choline ⁹ (β-hydroxyethyltrimethylammonium hydroxide)	 $C_5H_{15}NO_2$ Mol. wt. 121.18 M.p. 180 °C (decomp.)	Component of lecithin, plasmalogens, distributed in plants and animals (egg-yolk 17, meat 6, cereals 1mg per gramme). See also pages 394 and 434	Methyl-group replaceable by of labile met when synth the latter involved in fatty acids f to periphers
α-Lipoic acid ¹¹ (thioctic acid)	 $C_8H_{14}O_2S_2$ Mol. wt. 206.33 M.p. 48 °C	In small amounts in vegetable and animal tissues, particularly yeasts and liver	Involved in decarboxylation and acids (see 391)
Essential fatty acids ¹² (vitamin F)	Linoleic and arachidonic acids (see page 370) Unsaturated fatty acids and related compounds such as the corresponding alcohols not synthesized by the body in adequate quantity but necessary for metabolism and growth	In the diet, particularly linoleic acid (plant oils, animal fats) and arachidonic acid (animal fats). Also active are linoleic acid precursors such as linoleyl alcohol and cis-2-octenic acid ¹³ ; linolenic acid is almost inactive. Arachidonic acid is synthesized in the animal body from linoleic acid	Involved in the cell membrane possibly triglycerides. Structural components of prostaglandins of prostaglandin synthetase in mitochondria and fatty acids and arachidonic acid but also effect on the release of cholesterol

* See footnote, page 491.

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(For references see page 497)

A *nutritional standard* is a statement of the amounts of certain nutrients (usually the average daily amounts) regarded as necessary for a person representative of the category of the population to which the standard applies¹. Terms such as *nutritional requirement* and *nutritional allowance* are also used but must not always be regarded as synonymous. The resulting diets are referred to as minimum, average or desirable. Since it is at present impossible to define an individual's optimum requirement of any dietary constituent, other methods of evaluating nutritional standards have become necessary. In USA, the recommended dietary allowances² are

Recommended daily allowances of calories (FAO³) and of vitamin A (retinol), thiamine, riboflavin and niacin* (Joint FAO/WHO Expert Group⁴)

Age	Calories per day	Retinol ¹ (mg)	Thiamine (mg)	Riboflavin (mg)	Niacin equivalents ^{1†}
0-3 months**	120 per kg	-	-	-	-
4-6 months**	110 per kg	-	-	-	-
7-12 months	1000	300	0.4	0.6	6.6
1 year	1150	250	0.5	0.6	7.6
2 years	1300	250	0.5	0.7	8.6
3 years	1450	250	0.6	0.8	9.6
4-6 years	1700	300	0.7	0.9	11.2
7-9 years	2100	400	0.8	1.2	13.9
10-12 years	2500	575	1.0	1.4	16.5
13-15 (boys)	3100	725	1.2	1.7	20.4
(girls)	2600	725	1.0	1.4	17.2
16-19 (boys)	3600	750	1.4	2.0	23.8
(girls)	2400	750	1.0	1.3	15.8
Adults (men)	3200	750	1.3	1.8	21.1
(women)	2300	750	0.9	1.3	15.2

* For diets containing both carotene and retinol, adjustments must be made as follows: recommended intake of mixed vitamin A active compounds =

$$\frac{\text{recommended intake of retinol}}{0.167k + (1-k)}, \text{ where } k = \frac{\beta\text{-carotene } (\mu\text{g})}{\beta\text{-carotene } (\mu\text{g}) + \text{retinol } (\mu\text{g})}$$

† A niacin equivalent is 1 mg niacin or 60 mg L-tryptophan

Daily protein requirements (FAO/WHO Expert Group⁴)

Age	Gramme Reference Protein* per kilogramme body weight	
	Average	Range**
Infants*		
0-3 months	2.3	-
3-6 months	1.8	-
6-9 months	1.5	-
9-12 months	1.2	-
Juveniles		
1-3 years	0.83	0.70-1.06
4-6 years	0.81	0.65-0.97
7-9 years	0.77	0.62-0.92
10-12 years	0.72	0.58-0.86
13-15 years	0.70	0.56-0.84
16-19 years	0.64	0.51-0.77
Adults**	0.59	0.47-0.71

* The composition of the Reference Protein is given on page 516. The proteins of eggs, milk and meat all have the same biological value. The intake of proteins of lower biological value must be correspondingly increased.

** This range is based on the expected range of individual variation; the upper level is likely to cover the requirements of 95% of the population.

Desirable daily calcium allowances (FAO/WHO Expert Group⁴)

Age	mg/day
0-12 months*	500-600
1-9 years	400-500
10-15 years	600-700
16-19 years	500-600
Adults	400-500
Pregnancy, 3rd trimester	1000-1200
Lactation	1000-1200

* For infants not being breast fed, the calcium requirement of an infant being breast fed by a normally lactating mother is met by the breast milk.

Calories¹

The body requires food energy for resting metabolism, synthesis of body tissues, physical activities, excretory processes and maintenance of thermal balance. The energy requirements at different levels of activity are given in the tables on page 495.

Recommended daily dietary allowances* (Food and Nutrition Board, USA²)

	Age** (years)	Weight		Height		Calories (kcal)	Protein (g)	Minerals				
		(kg)	(lb)	cm	(in)			Calcium (g)	Phos- phorus (g)	Iodine (μg)	Iron (mg)	
Infants	0-1/2	4	9	55	22	kg × 120	kg × 2.2***	0.4	0.2	25	6	
	1/2-1	7	15	63	25	kg × 110	kg × 2.0***	0.5	0.4	40	10	
Children	1/2-1	9	20	72	28	kg × 100	kg × 1.8***	0.6	0.5	45	15	
	1-2	12	26	81	32	1100	25	0.7	0.7	55	15	
	2-3	14	31	91	36	1250	25	0.8	0.8	60	15	
	3-4	16	35	100	39	1400	30	0.8	0.8	70	10	
	4-6	19	42	110	43	1600	30	0.8	0.8	80	10	
	6-8	23	51	121	48	2000	35	0.9	0.9	100	10	
Males	8-10	28	62	131	52	2200	40	1.0	1.0	110	10	
	10-12	35	77	140	55	2500	45	1.2	1.2	125	10	
	12-14	43	95	151	59	2700	50	1.4	1.4	135	18	
	14-18	59	130	170	67	3000	60	1.4	1.4	150	18	
	18-22	67	147	175	69	2800	60	0.8	0.8	140	10	
	22-35	70	154	175	69	2800	65	0.8	0.8	140	10	
Females	35-55	70	154	173	68	2600	65	0.8	0.8	125	10	
	55-75+	70	154	171	67	2400	65	0.8	0.8	110	10	
	10-12	35	77	142	56	2250	50	1.2	1.2	110	18	
	12-14	44	97	154	61	2300	50	1.3	1.3	115	18	
	14-16	52	114	157	62	2400	55	1.3	1.3	120	18	
	16-18	54	119	160	63	2300	55	1.3	1.3	115	18	
	18-22	58	128	163	64	2000	55	0.8	0.8	100	18	
	22-35	58	128	163	64	2000	55	0.8	0.8	100	18	
	35-55	58	128	160	63	1850	55	0.8	0.8	90	18	
	35-75+	58	128	157	62	1700	55	0.8	0.8	80	10	
Pregnancy					+ 200	65	+0.4	+0.4	125	18		
Lactation					+ 1000	75	+0.5	+0.5	150	18		
		Fat-soluble vitamins				Water-soluble vitamins						
		Vitamin A activity (IU)	Vitamin D (IU)	Vitamin E activity (IU)	Ascorbic acid (mg)	Folacin† (mg)	Niacin†† (mEq)	Riboflavin (mg)	Thiamine (mg)	Vitamin B ₆ (mg)	Vitamin (μg)	
Infants	0-1/2	1500	400	5	35	0.05	5	0.4	0.2	0.2	1	
	1/2-1	1500	400	5	35	0.05	7	0.5	0.4	0.3	1	
Children	1/2-1	1500	400	5	35	0.1	8	0.6	0.5	0.4	2	
	1-2	2000	400	10	40	0.1	8	0.6	0.6	0.5	2	
	2-3	2000	400	10	40	0.2	8	0.7	0.6	0.6	2	
	3-4	2500	400	10	40	0.2	9	0.8	0.7	0.7	3	
	4-6	2500	400	10	40	0.2	11	0.9	0.8	0.9	4	
	6-8	3500	400	15	40	0.2	13	1.1	1.0	1.0	4	
Males	8-10	3500	400	15	40	0.3	15	1.2	1.1	1.2	5	
	10-12	4500	400	20	40	0.4	17	1.3	1.3	1.4	5	
	12-14	5000	400	20	45	0.4	18	1.4	1.4	1.6	5	
	14-18	5000	400	25	55	0.4	20	1.5	1.5	1.8	5	
	18-22	5000	400	30	60	0.4	18	1.6	1.4	2.0	5	
	22-35	5000	-	30	60	0.4	18	1.7	1.4	2.0	5	
Females	35-55	5000	-	30	60	0.4	17	1.7	1.3	2.0	5	
	55-75+	5000	-	30	60	0.4	14	1.7	1.2	2.0	6	
	10-12	4500	400	20	40	0.4	15	1.3	1.1	1.4	5	
	12-14	5000	400	20	45	0.4	15	1.4	1.2	1.6	5	
	14-16	5000	400	25	50	0.4	16	1.4	1.2	1.8	5	
	16-18	5000	400	25	50	0.4	15	1.5	1.2	2.0	5	
	18-22	5000	400	25	55	0.4	13	1.5	1.0	2.0	5	
	22-35	5000	-	25	55	0.4	13	1.5	1.0	2.0	5	
	35-55	5000	-	25	55	0.4	13	1.5	1.0	2.0	5	
	55-75+	5000	-	25	55	0.4	13	1.5	1.0	2.0	6	
Pregnancy		6000	400	30	60	0.8	15	1.8	+0.1	2.5	8	
Lactation		8000	400	30	60	0.5	20	2.0	+0.5	2.5	6	

* The allowance levels are intended to cover individual variations among most normal persons as they live in the USA under usual environmental stresses. The recommended allowances can be attained with a variety of common foods providing other nutrients for which human requirements have been less well defined.

** Entries on lines for age range 22-35 years represent the 'reference' man and woman at age 22 (see under 'Calories', page 493). All other entries represent allowances for the midpoint of the specified age range.

*** Assumes protein equivalent to human milk. For proteins not 100% utilized, factors should be increased proportionately.

† The folacin allowances refer to dietary sources as determined by *Lactobacillus casei* assay. Pure forms of folacin may be effective in doses less than a quarter of the recommended allowance.

†† Niacin equivalents include dietary sources of the vitamin itself plus 1 mEq for each 60 mg of dietary tryptophan.

Recommended daily calorie allowances (Food and Nutrition Board, 'ISA') (Light physical activity, mean environmental temperature 20°C)

	Body weight		RMR* at age 22	Age		
	(kg)	(lb)		22	45	65
Men	50	110	1540	2200	2000	1850
	55	121	1620	2350	2150	1950
	60	132	1720	2500	2300	2100
	65	143	1820	2650	2400	2200
	70	154	1900	2800	2600	2400
	75	165	1970	2950	2700	2500
	80	176	2020	3050	2800	2600
	85	187	2110	3200	2950	2700
	90	198	2210	3350	3100	2800
	95	209	2290	3500	3200	2900
Women	100	220	2380	3700	3400	3100
	40	88	1280	1550	1450	1300
	45	99	1380	1700	1550	1450
	50	110	1460	1800	1650	1500
	55	121	1560	1950	1800	1650
	58	128	1620	2000	1850	1700
	60	132	1640	2050	1900	1700
	65	143	1740	2200	2000	1850
	70	154	1830	2300	2100	1950

* RMR = resting metabolic rate, approximately 15% above the metabolic rate measured under basal conditions

Energy requirements during various activities*

Light work (2.5-4.9 kcal/min)	Moderately heavy work (5.0-7.4 kcal/min)	Heavy work (7.5-9.9 kcal/min)	Very heavy work (over 10 kcal/min)
Light industrial and domestic work	Farm work	Mine- working	Felling trees
Gymnastics	Marching with rucksack	Playing football	Steelmaking
Tile-laying	Ballroom dancing		Swimming (crawl)
Painting	Playing tennis		Climbing
Tending agricul- tural machines	Cycling		
Driving goods vehicles			
Playing golf, bowling			

unreasonably heavy clothing is worn. The calorie requirement in-

Normal energy requirements of recumbent adults*

Body weight (kg)	Body type	Energy requirement (kcal/min)									
		45	50	55	60	65	70	75	80	85	90
5-9	Lean	-	-	0.99	1.06	1.12	1.19	1.26	1.32	1.39	-
10-14	Average	-	-	0.94	1.01	1.09	1.14	1.21	1.28	1.34	-
15-19	Heavily built	-	-	0.82	0.89	0.96	1.03	1.09	1.16	1.23	1.30
20-24	Cor- pulent	-	-	0.78	0.84	0.91	0.98	1.05	1.11	1.18	1.25
25-29	Heavily built	-	-	0.80	0.86	0.93	1.00	1.07	1.13	1.20	-
>30	Cor- pulent	-	-	0.81	0.88	0.95	1.02	1.08	1.15	-	-

Normal energy requirements of adults sitting and at rest*

Age in years	Number of subjects	Energy requirement (kcal/min)		
		Mean	Range	t
Men (65 kg = 143 lb)				
20-39	30	1.39	0.97-1.79	0.25
40-64	30	1.37	0.87-1.94	0.29
65 and over	23	1.29	0.91-1.94	0.25
Women (55 kg = 121 lb)				
20-39	30	1.15	0.75-1.63	0.23
40-59	30	1.07	0.73-1.56	0.19
60 and over	23	1.09	0.77-1.62	0.31

Normal energy requirements of adults during walking*

Body weight (kg)	Rate of walking (km/h)	Energy requirement (kcal/min)							
		45	50	55	60	65	70	75	80
3	1.9	2.1	2.5	2.8	3.2	3.5	3.8	4.1	4.4
4	2.5	2.7	3.2	3.6	4.0	4.3	4.6	4.9	5.2
5	3.1	3.2	3.7	4.2	4.7	5.1	5.5	5.9	6.3
6	3.7	3.8	4.4	4.9	5.4	5.9	6.4	6.9	7.4
7	4.3	4.4	5.0	5.5	6.1	6.6	7.1	7.6	8.1

allowance* is between 2.5 g and a maximum of 6 g per kilogram of body weight per day.

Carbohydrate and fat*

The desirable intake of carbohydrate and fat, like the appropriate composition of foods, is difficult to assess. Apart from the body's specific needs for carbohydrate (e.g., brain energy), fat and fat appear to be interchangeable as dietary energy sources, as in the body they are interconvertible, except that fatty acids in an even number of Carbons from coconut fat, etc. cannot be used form carbohydrate. Adaptation to diets very low in carbohydrates is possible, but for persons accustomed to a normal diet at least 100 g carbohydrate per day appears to be necessary if mental disturbances like ketosis, excessive protein breakdown, etc. are avoided. Normal intake is...

this page

Protein

Dietary protein is the source of the nitrogen and essential amino

for food protein, is 0.9 g protein per kilogramme body weight per day, a value about nine times the minimum requirement of Reference Protein*. In the case of infants it is assumed that when lactation is normal sufficient protein is obtained from the breast milk, even though this provides little more than the minimum requirement. For the protein allowances recommended by the FAO/WHO Expert Group see page 473. For premature infants the recommended

can be prevented by ensuring that the amount of this substance in the formula supplies 3% of the calories¹⁰.

Essential amino acids

Of the 18 amino acids contained in food proteins 8 are essential in that the body is not capable of synthesizing them (tryptophan, phenylalanine, lysine, threonine, methionine, leucine, isoleucine, valine), 2 are semi-essential in that they are not synthesized in adequate amounts during growth (histidine, arginine), and 6 are non-essential in that the body can synthesize them from a nitrogen source such as any amino acid, ammonium salts or urea (aspartic acid, glutamic acid, proline, glycine, serine, alanine).

Requirements of the essential amino acids*

Amino acid	Infants Minimum requirement ¹¹ (mg/kg/day)	Adults**		Recommended intake ¹² (g/day)
		Young men ¹² (g/day)	Young women ¹³ (g/day)	
L-Histidine	34	0	0	0
L-Tryptophan	22	0.25	0.16	0.50
L-Phenylalanine				
Tyrosine available†	90	0.30	0.22	—
Tyrosine not available ...	—	1.10	—	2.20
L-Lysine	103	0.80	0.50	1.60
L-Threonine	87	0.50	0.31	1.00
L-Methionine				
Cystine available††	45	0.20	0.35	—
Cystine not available ...	—	1.10	—	2.20
L-Leucine	150	1.10	0.62	2.20
L-Isoleucine	126	0.70	0.45	1.40
L-Valine	105	0.80	0.65	1.60

* Assuming that the nitrogen intake is adequate for the formation of the non-essential amino acids.

** The requirements are higher during pregnancy and lactation. The minimum requirement of men over 50 is higher than that of young men in respect of at least two amino acids (methionine 2.4–3.0 g/day, lysine 1.4–2.8 g/day)¹⁴.

† 70–75% of the phenylalanine requirement can be met by tyrosine¹².

†† 80–90% of the methionine requirement can be met by cystine¹².

Water

The water requirement of the body is determined by the amount of heat it produces and by the load of solutes in the body fluids. It is closely linked to the intake of salt. The intake must replace water losses in the urine, faeces, sweat and insensible perspiration (skin and lungs). Under the most favourable conditions (low-solute diet, resting, no sweating) the total water supplied by the diet and metabolic processes should be at least 1.5 l/day¹⁵. A reasonable water allowance is 1 ml per calorie of food². In hot, dry climates the water requirement can be considerably increased as a result of sweating. Under ordinary conditions, infants require proportionately more water than adults and should be given 1.5 ml per calorie of food².

See also 'Water and Electrolyte Balance', pages 523–530.

Sodium and chloride

The requirement of sodium and chloride is closely linked to the water balance of the body. Both the total body content and body-fluid concentration of sodium are homeostatically controlled, moderate intakes being rapidly excreted in the urine while a reduction in intake causes excretion to drop quickly to a very low level¹⁶. Sodium deficiency is rare in healthy persons provided there is no abnormal loss. The normal recommended NaCl intake is 1 g per kilogramme of water². Hard physical work in the tropics would require a daily intake of up to 19 g NaCl¹⁷. Normal diets in western Europe and USA contain 6–18 g NaCl.

Potassium

The minimum daily potassium requirement probably amounts to 0.8–1.3 g². Normal diets in western countries provide 0.8–1.5 g potassium per 1000 kcal. An adequate potassium intake is important during prolonged intravenous feeding, recovery from severe

diarrhoea, and diabetic acidosis; this should be met by an int 40–120 mg (1–3 mEq) per kg body weight per day.

Magnesium

The probable daily magnesium requirement¹⁸ is 150 rr children under 10 years and 200–300 mg for older children a daily protein intake of 70–80 g, men require 300–400, w 300 mg per day. The requirement seems to increase with incre protein intake. For the recommendations of the Food and Nutrition Board (USA) see the table on page 494. An average diet provides 250–500 mg magnesium per day.

Calcium and phosphorus

Knowledge of the minimum requirements of calcium is inadequate, but it is well established that no injurious effects occur if the daily calcium intake lies between 300 mg and 2000 mg¹⁹.

The desirable calcium intakes (*suggested practical allowance*) commended by the FAO/WHO Expert Group (see table on 493) are lower than those of the Food and Nutrition Board (U see table on page 494).

Although the calcium-phosphorus ratio in bone is 2:1 it is lower in the soft tissues. This, and the fact that on a normal the intake of phosphorus always equals or exceeds that of calcium have led to the recommendation² that the calcium and phosph allowances should be equal except in the case of young infants the table on page 494).

Iron

In order to remain in iron balance, the daily iron intake of men as well as of women after the menopause, must be 0.5–1.0 mg per day. Menstruating women require some 0.3–1.0 mg per day more. The iron requirement is increased during pregnancy, particularly as a result of the increase in the total erythrocyte volume, and need is met partly by mobilization of iron reserves. The latter is restored post partum when the total erythrocyte volume falls again.

During the first months of life the iron requirement of infants is met principally from endogenous sources. Special attention should be paid to the iron needs of growing girls, who have to meet not only the requirements of growth but also cover menstruation losses. Assuming that 10% of the dietary iron is absorbed, the following amounts must be available in the diet:

Dietary iron requirements (Committee on Iron Deficiency American Medical Association²¹)

	Iron requirement of body mg/day	Dietary iron content* mg/day
Men	0.5–1.0	5–10
Menstruating women	0.7–2.0	7–20
Pregnant women	2.0–4.8	20–48
Adolescents	1.0–2.0	10–20
Children	0.4–1.0	4–10
Infants	0.5–1.5	1.5 mg/kg

* Assuming 10% absorption of dietary iron.

** Up to a maximum of 15 mg.

With the exception of those during pregnancy, these requirements are almost identical with the recommendation of the Food and Nutrition Board (USA) (page 494).

Estimates of dietary iron intake in the UK, USA, Australia and Canada have given values of 10–20 mg per person per day; various studies in the USA have shown that children aged 3–6 years have a daily iron intake of 3–11 mg²².

In infants the iron requirement is not met by the normal intake of breast or cow's milk alone. Premature infants, as well as infants with iron deficiency, require additional iron from the 2nd to 3rd month of life on; this should be given in the form of enriched cereals or possibly iron salts²³. The iron requirement in pregnancy is likewise met only with difficulty from dietary sources.

Copper

Copper is an important component of various enzymes involved in oxygen transport. In USA and Europe the diet of adults contains an average of 1–5 mg copper per day²². The daily requirement of adults has been estimated at 1.5–2 mg²², that of infants and children at 0.04–0.14 mg per kilogramme body weight²⁴.

can be prevented by ensuring that the amount of this substance in the formula supplies 3% of the calories¹⁰.

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Of the 18 amino acids contained in food proteins 8 are essential in that the body is not capable of synthesizing them (tryptophan, phenylalanine, lysine, threonine, methionine, leucine, isoleucine, valine), 2 are semi-essential in that they are not synthesized in adequate amounts during growth (histidine, arginine), and 6 are non-essential in that the body can synthesize them from a nitrogen source such as any amino acid, ammonium salts or urea (aspartic acid, glutamic acid, proline, glycine, serine, alanine).

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		Minimum requirement		Recommended intake ¹²
		Young men ¹² (g/day)	Young women ¹² (g/day)	(g/day)
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In order to remain in iron balance, the daily iron intake of men, as well as of women after the menopause, must be 0.5–1.0 mg; menstruating women require some 0.3–1.0 mg per day more²⁰. The iron requirement is increased during pregnancy, particularly as a result of the increase in the total erythrocyte volume, and this need is met partly by mobilization of iron reserves. The latter are restored post partum when the total erythrocyte volume falls again.

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Copper

Copper is an important component of various enzymes involved in oxygen transport. In USA and Europe the diet of adults contains an average of 1–5 mg copper per day²⁴. The daily requirement of adults has been estimated at 1.5–2 mg^{2,25}, that of infants and children at 0.04–0.14 mg per kilogramme body weight²⁶.

Amounts of principal nutrients, vitamins and minerals in various foods (tables on pages 499-515)

The extensive literature available on the chemical composition of foods has necessitated a critical selection of the most reliable and representative values for the various nutrients. The principal tables that have been made use of are those of the FAO¹, the US Department of Agriculture², the British Medical Research Council³ and the West German Bundesministerium für Ernährung, Landwirtschaft und Forsten⁴. Data from various journals⁵ have also been made use of. Detailed summaries of the nutrient contents of foods are also to be found in the works compiled by CHURCH and CHURCH⁶, the Swiss Lebensmittelbuchkommission⁷, RANDOIN et al.⁸, SCHALL⁹ and SCHTENBERG et al.¹⁰, as well as in the monographs of ALBRITTON¹¹, MATTICE¹², PROUDFIT and ROBINSON¹³, TURNER¹⁴, and others.

It is important to note that the actual concentration of a particular substance in a foodstuff can deviate from the value given in the tables since all foods are subject to large variations in composition. This is particularly the case with prepared foods such as preserves, chocolate, sausages, etc. With meat, the degree of fattening of the animal plays an important part (fat content), with vegetable foods the climate, nature of the soil and degree of ripening. The storage conditions of foods affect the extent to which their water and vitamin contents are conserved. Water loss results in a higher concentration of all nutrients.

Preparing and cooking foods can lead to loss of nutrients. Some vitamins are decomposed by heat and oxidation. Both vitamins and mineral constituents pass into water in which foods are cooked and are lost if this is discarded.

The values given in the food composition tables are the contents in 100 g of the edible portion, uncooked unless otherwise stated.

With the exception of the calorific value, the data indicate the total amounts of the components in the food as ingested and not in that part of it absorbed. Little is known of the extent to which minerals and vitamins are absorbed. Thus only 2-12% - depending on the type of foodstuff - of the iron contained in foods is absorbed; the element is more readily absorbed from lean meat, haemoglobin and soya beans than from eggs, cereals and vegetables¹⁵. A high oxalic acid content can seriously interfere with the absorption of calcium.

The *water content* is usually determined by measuring the loss of weight at high temperature, so that the values may include other readily volatile substances.

The *protein content* is obtained from the nitrogen content by multiplying by 6.25 for meat and eggs, by 6.38 for milk, and by various factors ranging from 5.18 to 6.25 for vegetables, cereals and nuts (for details see the US Department of Agriculture Handbook No. 8²).

The *fat content* is that part of the food extractable by fat solvents (for instance ether). The data for polyene fatty acids are either the sum of the linoleic and arachidonic acid contents or the difference between the oleic acid and total unsaturated fatty acid contents. The cholesterol content is roughly equivalent to the unsaponifiable part of the total fat. Cholesterol occurs only in animal products, however, so that 'cholesterol' values for nuts, cereals and other vegetable foods reflect their content of other sterols.

The *carbohydrate content* is usually determined by difference, namely as the total weight less water, protein, fat and ash. Data for fibre content vary greatly with the method of determination. Collected data on the amounts of the various carbohydrates in foods are available¹⁶.

The *calorific value* is calculated from the fat, carbohydrate and protein (and any alcoholic) content by using a specific factor that takes account of the varying extent to which different foods are absorbed (for details see the report by the Food and Agriculture Organization¹⁷); the data therefore represent utilizable calories.

Vitamins. Amounts of vitamin A (including β -carotene) and vitamin D are given in international units (IU), those of all other vitamins in milligrammes. 1 IU vitamin A = 0.0003 mg vitamin A or 0.0006 mg β -carotene; 1 IU vitamin D = 0.000025 mg vitamin D. The data under vitamin E are α -tocopherol values (when known) since this compound is responsible for most of the vitamin activity (see page 465).

Percentage vitamin losses during cooking¹⁸

	B ₁	B ₂	Nicotinic acid
Meats	35	20	25
Meats plus drippings	25	5	10
Eggs	25	10	0
Cereals	10	0	10
Legumes	20	0	0
Vegetables (leafy, green and yellow)	40	25	25
Vegetables, other	25	15	25
Tomatoes	5	5	5
Potatoes	40	25	25

Zero and unknown values. Zero values are indicated by 0 through a dash (-) denotes that the value is unknown.

References

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Fruits, Fruit Juices	Water	Proteins	Total	Poly-unsaturated	Carbo- hydrate	Calorie*	Vitamins						Other vitamins**		Organic constituents		Elements																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																					
							A**	B ₁	B ₂	B ₆	Niacin	Ascorbic	C	Malic acid	Citric acid	Oxalic acid	Ascorbic acid	Na	K	Ca	Mg	Mn	Fe	Cu	P	S	Chlorine																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																											
Content per 100 grammes soluble portion (unless otherwise stated)	g	g	g	g	g	kcal	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg

* Wide variations between different varieties.

** Highly coloured variety.

* Whole variations between different varieties.

** Highly coloured variety.

*** FA = folic acid, E = ascorbic acid, unless otherwise stated.

**** FA = folic acid, E = ascorbic acid, unless otherwise stated.

***** FA = folic acid, E = ascorbic acid, unless otherwise stated.

***** FA = folic acid, E = ascorbic acid, unless otherwise stated.

Content per 100 grammes edible portion (unless otherwise stated)	Water g	Proteins		Fats		Carbo- hydrates		Calories* kcal	Vitamins							Other organic constituents			Elements												
		g	%	Total g	Poly- unsaturated g	Total g	Fibre g		A** IU	B ₁ mg	B ₂ mg	B ₆ mg	Nicotinic acid mg	Pantothenic acid mg	C mg	Other vitamins*** mg	Malic acid mg	Citric acid mg	Oxalic acid mg	Excess acid A	Excess base B	Na mg	K mg	Ca mg	Mg mg	Manga- nese mg	Fe mg	Cu mg	P mg	S mg	Cl mg
Currents red and white (<i>Ribes rubrum</i>) ...	85.7	1.4	0.2	-	-	12.1	3.4	50	120	0.04	0.02	0.05	0.3	0.06	41	biotin 0.0026	50	2300	19	B	B	2	275	36	15	0.6	1.0	0.12	23	29	13
black (<i>Ribes nigrum</i>)	82	1.0	0.1	-	-	16.1	5.7	62	220	0.05	0.03	0.08	0.3	-	136	-	400	3030	4	B	B	3	336	17	10	-	0.9	0.12	28	-	-
Dates (<i>Phoenix dactylifera</i>) dried	22.5	2.2	0.5	-	-	72.9	2.3	274	50	0.09	0.10	0.1	2.2	0.8	0	FA 0.025	-	-	-	B	B	1	790	59	65	0.15	3.0	0.21	63	65	290
Elderberries, black (<i>Sambucus nigra</i>) dried	80.9	2.5	0.5	-	-	15.9	6.8	42	600	0.07	0.08	0.25	1.5	0.18	18	biotin 0.002; FA 0.017	-	-	-	B	B	0.5	305	35	-	-	1.6	-	57	-	-
Figs (<i>Ficus carica</i>)	81.7	1.2	0.4	-	-	16.1	1.4	65	75	0.09	0.08	0.13	0.63	0.4	2	FA 0.01	trace	340	-	B	B	2	190	35	21	-	0.8	0.06	22	12	14
dried	23.0	4.3	1.3	-	-	69.1	5.6	274	80	0.10	0.10	0.32	1.7	0.5	0	FA 0.03	-	-	-	B	B	34	780	126	82	0.35	4.0	0.35	116	69	105
Fruit cocktail canned	79.6	0.4	0.1	-	-	19.7	0.4	76	140	0.02	0.01	-	0.4	-	2	-	-	-	-	B	B	5	160	9	8	-	0.4	0.03	12	2	3
Gooseberries (<i>Ribes grossularia</i>) ..	88.9	0.8	0.2	-	-	9.7	1.9	39	290	0.15	0.03	0.02	0.3	0.15	25	biotin 0.0005	500- 2080	-	-	B	B	1	210	35	9	0.04	0.5	0.08	31	15	9
Grapes (<i>Vitis vinifera</i>)	81.4	0.6	0.3	-	-	17.3	0.5	67	100	0.05	0.02	0.1	0.3	0.08	4	biotin 0.002; FA 0.006	650	-	-	B	B	2	250	12	7	0.083	0.4	0.1	20	9	2
Grape juice	82.9	0.2	trace	-	-	16.6	trace	66	-	0.04	0.02	0.021	0.2	0.04	2	biotin 0.0003; FA 0.003	310	20	-	B	B	1	120	11	4	-	0.3	0.02	12	-	-
Grapefruit (<i>Citrus decumana</i>)	88.4	0.6	0.1	-	-	9.8	0.5	39	80	0.04	0.02	0.02	0.2	0.25	40	E 0.25; FA 0.003; biotin 0.003	80	1460	0	B	B	2	198	17	10	0.01	0.3	0.02	16	5	3
per lb at purchase (refuse 51%)...	197	1.3	0.2	-	-	22	1.1	87	178	0.09	0.04	0.04	0.4	0.56	89	E 0.56; FA 0.002; biotin 0.007	178	3250	0	B	B	5	441	38	22	0.02	0.7	0.04	36	11	7
canned, sweetened	81.1	0.6	0.1	-	-	17.8	0.2	70	10	0.03	0.02	-	0.2	-	30	-	-	-	-	B	B	2	135	13	11	-	0.3	-	14	-	-
Grapefruit juice, fresh	89.2	0.4	0.1	-	-	9.8	0.1	41	10	0.03	0.02	0.014	0.2	0.16	45	biotin 0.0007; FA 0.001	-	-	-	B	B	2	150	8	12	-	0.4	-	14	5	2
Lemons (<i>Citrus medica</i>)	90.1	1.1	0.3	-	-	8.2	0.4	27	20	0.04	0.02	0.06	0.1	0.2	45	FA 0.007	trace	3840	-	B	B	6	148	26	9	0.04	0.6	0.26	16	8	4
Lemon juice	91.0	0.5	0.2	-	-	8.0	-	25	20	0.03	0.01	0.039	0.1	0.1	50	FA 0.001	290	6080	-	B	B	1	130	14	7	-	0.2	0.13	11	2	4
Lime juice (<i>Citrus aurantiifolia</i>) ...	90.3	0.3	-	-	-	9.0	-	26	10	0.02	0.01	0.05	0.1	-	32	-	-	-	-	B	B	1	100	9	-	-	0.2	-	11	-	39
Loquats (<i>Eriobotrya japonica</i>) var. Loughberries (<i>Rubus urticae</i> var. Loughberries)	83	1.0	0.6	-	-	14.9	3.0	62	200	0.03	0.04	-	0.4	-	24	-	-	-	-	B	B	1	170	35	25	-	1.2	0.14	17	18	16
Melons, water (<i>Citrullus vulgaris</i> var. <i>cylindricus</i>)	92.6	0.5	0.2	-	-	6.4	0.3	26	590	0.03	0.03	0.033	0.2	0.3	7	biotin 0.004; FA 0.0006	200	-	0	B	B	0.3	100	7	8	0.02	0.5	0.07	10	9	8
Nectarines (<i>Prunus persica</i> var. <i>nectarina</i>)	81.8	0.6	trace	-	-	17.1	0.4	64	1650	-	-	-	-	-	13	-	-	-	-	B	B	6	294	4	13	-	0.5	0.06	24	10	5

* To convert to kJ (kilojoule) multiply the values given by 4.1855. ** Vitamin A. *** Vitamins.

* To convert to kJ (kilojoule) multiply the values given by 4.1855. ** Vitamin A content given by 4.1855.

Content per 100 grammes edible portion (unless otherwise stated)	Water g	Proteins		Fats		Carbo- hydrates		Calories* kcal	Vitamins						Other organic constituents			Excess base A B	Elements												
		g	g	Total g	Poly- unsaturated g	Total g	Fibre g		A** IU	B ₁ mg	B ₂ mg	B ₆ mg	Nicotinic acid mg	Pantothenic acid mg	C mg	Other vitamins** mg	Malic acid mg		Citric acid mg	Oxalic acid mg	Na mg	Potas- sium mg	Calcium mg	Magne- sium mg	Manga- nese mg	Fe mg	Cu mg	Phos- phorus mg	S mg	Cl mg	
Chives (<i>Allium schoenoprasum</i>)	91.3	1.8	0.3	-	-	5.8	1.1	28		5800	0.04	0.11	-	0.3	-	22	-	-	1.1	B	3	250	76	32	-	0.9	0.11	26	-	-	
Corn (sweet). See Maize																															
Cress, garden (<i>Lepidium sativum</i> ssp. <i>sativum</i>)	89.4	2.6	0.7	-	-	5.5	1.1	32		9300	0.08	0.26	-	1.0	-	69	-	-	-	B	14	606	81	-	-	1.3	-	76	-	-	
Cucumbers (<i>Cucumis sativus</i>)	95.6	0.8	0.1	-	-	3.0	0.6	13		300	0.04	0.05	0.04	0.2	0.3	8	biotin 0.001; FA 0.001	240	10	25	B	5	140	25	9	0.15	1.1	0.06	27	12	30
per lb as purchased (refuse 5%)	412	3.4	0.4	-	-	13	2.6	56		1290	0.17	0.22	0.17	0.9	1.3	34	biotin 0.004; FA 0.004	1030	43	108	B	22	603	108	39	0.65	4.7	0.26	116	52	129
Dandelion greens (<i>Taraxacum</i> <i>officinale</i>)	85.6	2.7	0.7	-	-	9.2	1.6	45		14000	0.19	0.26	-	-	-	36	-	-	25	B	76	430	187	-	0.3	3.1	0.15	66	17	99	
Eggplants (<i>Solanum melongena</i>)	92.4	1.2	0.2	-	-	5.6	0.9	25		10	0.05	0.05	-	0.6	0.23	5	-	170	0	6.9	B	0.9	190	17	10	0.11	0.4	0.08	26	9	24
Endives (<i>Cichorium endivia</i>)	93.1	1.7	0.1	-	-	4.1	0.9	20		3300	0.10	0.20	-	0.72	-	10	-	-	27.3	B	18	400	104	13	0.22	1.7	0.09	38	26	71	
Fennel (<i>Foeniculum vulgare</i>)	90	1.5	0.1	-	-	6.4	0.5	27		3500	0.23	0.11	0.10	0.2	0.25	31	FA 0.1; biotin 0.003	-	-	-	B	331	784	100	-	-	2.7	-	51	-	-
Garlic (<i>Allium sativum</i>) bulbs	63.8	5.3	0.2	-	-	29.3	1.1	129		trace	0.21	0.08	-	0.6	-	9	-	-	-	B	32	515	38	36	-	1.4	-	134	-	-	
Horse-radishes (<i>Armoracia lapathi- folia</i>)	76.6	2.8	0.3	-	-	18.1	2.8	80		30	0.06	0.11	0.18	0.6	-	120	-	-	-	B	9	554	105	33	-	2.0	0.14	70	212	18	
Kale (<i>Brassica oleracea</i> var. <i>acephala</i>)	87.5	4.2	0.8	-	-	6.0	1.3	38		8900	0.16	0.26	0.19	2.0	0.1-1.4	115	E 8; biotin 0.0005; FA 0.05	50	350	13	B	75	410	179	37	0.5	2.2	0.09	73	115	122
Kohlrabi (<i>Brassica oleracea</i> var. <i>gongylodes</i>), tubers	90.3	2.0	0.1	-	-	6.6	1.0	29		20	0.06	0.04	0.12	0.3	0.1	53	FA 0.01	-	-	-	B	10	392	41	48	0.11	0.5	0.14	51	-	57
Leeks, leaves (<i>Allium porrum</i>)	87.8	2.0	0.3	-	-	9.4	1.2	44		50	0.06	0.04	-	0.5	-	18	E 1.0	-	-	-	B	5	300	60	18	0.07	1.0	0.3	50	72	40
Lentils, dried (<i>Lens esculenta</i>)	11.1	24.7	1.1	-	-	60.1	3.9	340		60	0.50	0.25	0.49	2.0	1.5	-	biotin 0.013; FA 0.1	-	-	-	B	36	810	79	77	-	8.6	0.7	377	122	64
Lettuce (<i>Lactuca sativa</i>), headed . . .	95.1	1.3	0.2	-	-	2.5	0.5	14		970	0.06	0.07	0.07	0.3	0.1	8	E 0.6; biotin 0.003; FA 0.02	170	20	7.1	B	12	140	35	10	0.80	2.0	0.07	26	12	39-74
Maize (<i>Zea mays</i>)	72.7	3.5	1.0	-	-	22.1	0.7	96		400	0.15	0.12	0.22	1.7	0.89	12	biotin 0.006; FA 0.03	0	0	5.2	B	0.4	300	3	38	0.15	0.7	0.06	111	32	14
canned, drained solids	75.9	2.6	0.8	-	-	19.8	0.8	84		350	0.03	0.05	0.27	0.9	0.28	4	biotin 0.003; FA 0.008	-	-	-	B	2362	97	5	19	-	0.5	-	49	-	-
Mushrooms (champignons) (<i>Pleurotus campestris</i>)	90.8	2.8	0.24	-	-	3.7	0.9	22		0	0.1	0.44	0.05	6.2	2.1	5	E 0.834; biotin 0.016; FA 0.03; FA 150 IU	-	-	-	B	5	520	9	13	0.08	0.8	1.8	116	34	25

Vegetable	Ascorbic acid, mg	Thiamine, mg	Riboflavin, mg	Niacin, mg	Pyridoxine, mg	Folate, mg	Vitamin A, IU	Vitamin B ₁₂ , µg	Calcium, mg	Iron, mg	Copper, mg	Phosphorus, mg	Sulphur, mg	Chlorine, mg
<i>Onions (Allium cepa)</i>														
type	891	1.5	0.1	-	-	-	87	0.4	38	40-005	0.04	0.1	0.2	0.17
dried	4	1.7	1.5	-	-	-	92.1	4.6	350	200	0.25	0.18	-	35
<i>Parsley (Petroselinum crispum)</i>														
851	3.4	0.6	-	-	-	-	850	0.15	44	8500	0.15	0.26	0.2	0.03
<i>Parsnips (Pastinaca sativa)</i>														
791	1.7	0.5	-	-	-	-	175	2.0	76	30-008	0.09	0.1	0.2	0.5
<i>Pears (Pyrus ussuriensis)</i>														
750	6.3	0.4	-	-	-	-	17.0	2.0	84	640	0.35	0.15	0.18	0.82
<i>Peas (Pisum sativum)</i>														
green, unripe	807	5.4	0.3	-	-	-	12.8	1.9	73	660	0.35	0.10	-	19
green, frozen	82.3	3.4	0.4	-	-	-	12.7	1.3	47	450	0.15	0.06	0.05	0.17
canned	9.3	24.2	1.0	-	-	-	62.7	1.2	348	120	0.87	0.25	0.05	3.0
<i>Peas, split</i>														
edible, podded	86.2	2.6	0.1	-	-	-	10.5	1.5	53	55	0.06	0.10	-	30
<i>Peppers (Capsicum spp.)</i>														
green chilies	92.8	1.2	0.2	-	-	-	5.3	1.4	24	420	0.06	0.08	-	128
<i>Potatoes (Solanum tuberosum)</i>														
raw	1.8	5.3	39.8	-	-	-	50.0	1.6	568	trace	0.21	0.07	-	16
<i>Potatoes (Solanum tuberosum)</i>														
raw	79.8	2.1	0.1	-	-	-	17.7	0.5	76	trace	0.15	0.04	0.2	0.3
<i>Potatoes (Solanum tuberosum)</i>														
raw	293	7.7	0.4	-	-	-	65	1.8	279	trace	0.41	0.15	0.7	7.3
<i>Potatoes (Solanum tuberosum)</i>														
per lb as purchased (refuse 19%)														
dried	71	8.3	0.6	-	-	-	80.4	1.4	352	trace	0.25	0.10	-	26
<i>Pumpkins (Cucurbita spp.)</i>														
95.0	0.8	0.1	-	-	-	-	3.5	0.6	15	1600	0.05	0.11	-	0.6
<i>Purslane (Portulaca oleracea)</i>														
var sativa	92.5	1.7	0.4	-	-	-	3.8	0.9	21	2500	0.05	0.10	-	25
<i>Radicchio (Eryngium yuccifolium)</i>														
93.7	1.1	0.1	-	-	-	-	3.6	0.7	18	10	0.04	0.04	0.1	0.3
<i>Rhubarb (Rheum palmatum)</i>														
94.9	0.5	0.1	-	-	-	-	3.8	0.7	16	100	0.01	0.03	0.03	0.1

* Unavailable

*** FA = folic acid, E = ascorbic acid, otherwise stated

* To convert to kJ (kilocalories) multiply the values given by 4.185
** Vitamin A activity: 1000 IU = 0.0005 µg retinol, 1000 IU = 0.0005 µg retinol, 1000 IU = 0.0005 µg retinol

Content per 100 grammes edible portion (unless otherwise stated)	Water	Proteins		Fats		Carbo- hydrates		Calories*	Vitamins						Other organic constituents			Elements												
		Total	Poly- unsaturated	Total	Fibre	A** IU	B ₁ mg		B ₂ mg	B ₆ mg	Nicotinic acid mg	Pantothenic acid mg	C mg	Other vitamins*** mg	Malic acid mg	Citric acid mg	Oxalic acid mg	Excess base B	Na Sodium mg	K Potas- sium mg	Ca Calcium mg	Magne- sium mg	Manga- nese mg	Fe mg	Copper mg	P Phos- phorus mg	S Sulphur mg	D Chlorine mg		
Rutabagas (<i>Brassica napus</i> var. <i>napobrassica</i>)	87.0	1.1	0.1	-	11.0	1.1	46	580	0.07	0.07	-	1.1	-	43	-	-	-	B	5	239	66	15	0.04	0.4	0.08	39	-	-	-	
Salsify (<i>Scorzonera hispanica</i>)	79	3.2	0.6	-	16.4	1.8	77	10	0.04	0.04	-	0.2	-	12	-	-	-	B	5	320	40	-	-	1.5	-	-	76	-	-	
Sauerkraut	92.8	1.0	0.2	-	4.0	0.7	18	50	0.03	0.04	-	0.2	0.08	14	-	-	-	B	650	140	36	-	-	0.5	0.1	18	-	-	-	
Soybeans (<i>Glycine hispida</i>), dried..	10.0	34.1	17.7	10.7	33.5	4.9	403	80	1.14	0.31	0.64	2.1	1.68	trace	E 6-11; biotin 0.06; FA 0.22	-	-	-	B	4	1900	226	235	-	8.4	0.11	554	-	-	-
Spinach (<i>Spinacia oleracea</i>)	90.7	3.2	0.3	-	4.3	0.6	26	8100	0.10	0.20	0.20	0.6	0.3	51	E 2.5; K 0.04-3; biotin 0.007; FA 0.075	90	80	460	B	62	662	106	62	0.82	3.1	0.20	51	27	65	
per lb at purchase (refuse 8%)....	379	13.4	1.3	-	17.9	2.5	109	33800	0.42	0.83	0.83	2.5	1.3	213	E 10.4; K 0.17-12.5; biotin 0.029; FA 0.031	376	334	1920	B	259	2760	442	259	3.42	12.9	0.83	213	113	271	
canned.....	93.0	2.0	0.4	-	3.0	0.7	19	5500	0.02	0.06	0.095	0.3	0.06	14	biotin 0.002; FA 0.05	-	-	364	B	320 ²	260	85	-	-	2.1	-	26	-	-	-
frozen	91.3	3.0	0.3	-	4.2	0.8	25	8100	0.1	0.16	-	0.5	-	35	-	-	-	-	B	53	385	105	-	-	2.5	-	45	-	-	-
Squash, summer (zucchini) (<i>Cucurbita pepo</i> var. <i>medullosa</i>) ..	94.6	1.2	0.1	-	3.6	0.6	17	320 ³	0.05	0.09	-	1.0	-	19	-	-	-	-	B	1	202	28	-	0.14	0.4	-	29	-	-	-
Sweet potatoes (<i>Ipomoea batatas</i>) ..	70.6	1.7	0.4	-	26.3	0.7	114	8800	0.10	0.06	0.32	0.6	0.03	21	E 4.0; biotin 0.004; FA 0.012	0	70	56	B	5	530	32	31	0.15- 0.52	0.7	0.15	47	15	85	
canned	70.7	1.0	0.2	-	27.5	0.6	114	5000	0.03	0.03	-	0.6	-	8	-	-	-	-	B	48	120	13	-	-	0.7	-	29	-	-	-
Tomatoes (<i>Lycopersicon esculentum</i>)	93.5	1.1	0.2	-	4.7	0.5	22	900	0.06	0.04	0.1	0.6	0.31	23	E 0.27; biotin 0.004; FA 0.008	150	390	7.5	B	3	268	13	11	0.19	0.6	0.10	27	11	51	
canned	93.7	1.0	0.2	-	4.3	0.4	21	900	0.06	0.03	0.07	0.7	0.2	17	biotin 0.0018; FA 0.003	-	-	-	B	130 ⁴	217	6	-	0.04	0.5	0.09	19	-	-	-
Tomato juice, canned	93.6	0.9	0.1	-	4.3	0.2	19	800	0.05	0.03	0.19	0.7	0.30	16	FA 0.007	23	336	-	B	230 ⁴	230	7	7	-	0.9	-	18	-	-	-
Tomato ketchup	68.6	2.0	0.4	-	25.4	0.5	106	1400	0.09	0.07	-	1.6	-	15	-	-	-	-	B	1042	363	22	21	-	0.8	-	50	-	-	-
Tomato puree	86.0	2.3	0.5	-	9.5	0.5	44	1200	0.09	0.06	0.18	1.5	-	9	-	-	-	-	B	590	1160	60	-	-	1.0	-	34	-	-	-
Turnips (<i>Brassica rapa</i>)	91.5	1.0	0.2	-	6.6	0.9	30	trace	0.04	0.07	0.11	0.6	0.02	36	E 0.02; biotin 0.0001; FA 0.004	230	0	0	B	37	230	39	7	0.04	0.5	0.07	30	22	41	
greens	90.3	3.0	0.3	-	5.0	0.8	28	7600	0.21	0.39	0.98	0.8	0.38	139	E 2.3; FA 0.04	-	-	15	B	10	440	260	19	1.4	1.8	0.09	58	54	168	
Watercress (<i>Nasturtium officinale</i>) ..	93.3	2.2	0.3	-	3.0	0.7	19	4000	0.1	0.27	-	0.9	0.1	75	-	-	-	-	B	60	301	151	17	0.54	2.0	0.04	46	147	109	

* To convert to kJ (kilojoules) multiply the values given by 4.1855.

** Vitamin A activity due to vitamin A + carotenes: 1 IU vitamin A = 0.0006

*** FA = folic acid; E = α-tocopherol unless otherwise stated.

* To convert to kJ (kilojoule) multiply the values given by 4.1855.

** Vitamin A activity due to vitamin A + carotenes; 1 IU vitamin A = 0.0006 mg *Retinol*.*** FA = folic acid; E = α -tocopherol unless otherwise stated.

2.15 mg/100 g

Content per 100 grammes edible portion (unless otherwise stated)	Water		Proteins		Fats		Carbo- hydrates		Vitamins						Other organic constituents			Elements																	
	g	%	g	%	Total	Poly- unsaturated	Total	Fibre	Calories*	IU	B ₁ mg	B ₂ mg	B ₆ mg	Nicotinic acid mg	Panto- thentic acid mg	C mg	Other vitamins***	Malic acid mg	Citric acid mg	Oxalic acid mg	Excess acid A	Excess base B	Na mg	Potas- sium mg	Ca mg	Magne- sium mg	Magne- nese mg	Fe mg	Cu mg	P Phos- phorus mg	S Sulphur mg	Cl Chlorine mg			
Bread (continued)																																			
pumpernickel.....	34.0	9.1	1.2	-	53.1	1.1	246			-	0.23	0.14	-	1.2	-	-	-	-	-	-	-	A	569	454	84	71	-	-	2.4	-	28	229	-	-	
rye, American.....	35.5	9.1	1.1	-	52.1	0.4	243			-	0.18	0.07	-	1.4	-	-	-	-	-	-	-	A	557	145	75	42	1.3	1.6	0.6	0.28	147	69	-	-	
zwieback.....	5.0	10.7	8.8	-	74.3	0.3	423			40	0.05	0.07	-	1.3	-	-	-	-	-	-	-	A	250	150	13	-	-	0.6	-	-	-	-	-	-	
Cornflakes.....	3.8	7.9	0.4	-	85.3	0.7	385			0	0.43 ¹	0.1	-	2.1	0.19	0	FA 0.006	-	-	-	5.6	A	660	160	10	17	0.05	1.4	0.17	45	93	-	-	-	
Cornstarch.....	12.0	0.3	trace	-	87.9	0.1	362			0	trace	0.08	0.005	0.03	-	-	-	-	-	-	-	A	4	4	trace	2	-	0.5	-	-	-	30	-	6	
Flour																																			
buckwheat.....	14.1	11.7	2.7	-	70	2.6	327			0	0.58	0.15	-	2.9	1.5	-	-	-	-	-	-	A	1	680	33	-	2.09	2.2	0.7	263	-	-	-	-	
farina, unenriched.....	10.3	11.4	0.9	-	77.0	0.4	371			0	0.06	0.10	-	0.7	-	-	-	-	-	-	-	A	2	83	25	25	-	1.5	-	-	107	-	-	-	
maize (corn).....	12.0	7.8	2.6	-	76.8	0.7	368			340 ²	0.20	0.06	0.06	1.4	0.55	0	biotin 0.006; FA 0.01; E 0.3	-	-	-	-	A	1	120	6	-	-	1.8	-	-	164	-	-	-	
rye, light.....	11	9.4	1.0	-	77.9	0.4	357			0	0.15	0.07	-	0.6	-	-	-	-	-	-	-	A	1	156	22	73	-	1.1	-	-	185	-	-	-	
rye, medium.....	11	11.4	1.7	-	74.8	1.0	325			0	0.30	0.12	-	2.9	-	-	-	-	-	-	-	A	1	203	27	83	-	2.6	-	-	262	-	-	-	
soybean, full fat.....	8.0	36.7	20.3	-	30.2	2.4	347			110	0.85	0.31	0.66	2.1	1.68	0	biotin 0.07; FA 0.43	-	-	-	-	B	-	1660	199	235	-	8.4	-	-	558	-	-	-	
medium fat.....	8.0	43.4	6.7	-	36.6	2.5	264			80	0.83	0.36	-	2.6	-	0	-	-	-	-	-	B	-	2025	244	286	-	9.1	-	-	634	-	-	-	
wheat, whole.....	12	13.3	2.0	-	71.0	2.3	333			0	0.55	0.12	-	4.3	-	0	-	-	-	-	-	A	3	370	41	113	-	3.3	0.2	372	-	-	-	-	
white, unenriched.....	12	10.5	1.0	-	76.1	0.3	363			0	0.06	0.05	-	0.9	-	0	-	-	-	-	-	A	2	95	16	25	-	0.8	-	-	87	-	-	-	
white, enriched.....	12	10.5	1.0	-	76.1	0.3	364			0	0.44	0.26	-	3.5	-	0	-	-	-	-	-	A	2	95	16	25	-	2.9	-	-	87	-	-	-	
white, self-raising, enriched.....	11.5	9.3	1.0	-	74.2	0.4	352			0	0.44	0.26	-	3.5	-	0	-	-	-	-	-	A	1079	90	265	-	2.9	-	-	466	-	-	-	-	
Muffins (enriched flour).....	38.0	7.8	10.1	-	42.3	0.1	294			100	0.17	0.23	-	1.4	-	trace	-	-	-	-	-	A	441	125	104	-	-	1.6	-	-	151	-	-	-	
Noodles, unenriched, dry.....	10.1	13.0	2.9	-	73	0.4	376			100	0.2	0.08	-	2.1	-	-	-	-	-	-	-	A	7	157	20	-	-	2.1	-	-	196	-	-	-	
Oatflakes.....	10.3	13.8	6.6	2.7	67.6	1.4	387			-	0.55	0.14	0.75	1.1	0.92	0	E 0.25	-	-	-	-	A	2	340	53	145	4.9	3.6	0.74	407	199	49	-	-	
Pancakes (enriched flour).....	50.1	7.1	7.0	-	34.1	0.1	231			120	0.17	0.22	-	1.3	-	trace	-	-	-	-	-	A	425	123	101	-	-	1.3	-	-	139	-	-	-	
Piecrust, plain, unenriched, unbaked.....	20.9	5.7	31.0	-	40.7	0.1	464			0	0.03	0.03	-	0.5	-	0	-	-	-	-	-	-	568	46	13	-	-	0.4	-	-	47	-	-	-	
Popcorn, popped.....	4.0	12.7	5.0	2.0	76.7	2.2	386			-	0.39	0.12	-	2.2	-	0	-	-	-	-	-	A	3	240	11	-	-	2.7	0.31	281	-	-	-	-	
Pretzels.....	4.5	9.8	4.5	-	75.9	0.3	390			0	0.02	0.03	-	0.7	-	0	-	-	-	-	-	A	1680	130	22	-	-	1.5	-	-	131	-	-	-	
Rice																																			
whole.....	12.0	7.5	1.9	-	77.4	0.9	360			0	0.29	0.05	-	4.7	-	0	E 1.2	-	-	-	-	A	9	150	32	119	1.7	1.6	0.36	221	121	-	-	-	
polished.....	12.0	6.7	0.4	-	80.4	0.3	362			0	0.07	0.03	0.15	1.6	0.63	-	E 0.35	-	-	-	-	A	6	113	24	28	1.08	0.8	0.06	94	79	27	-	-	
polished, cooked.....	72.6	2.0	0.1	-	24.2	0.1	109			0	0.02	0.01	-	0.4	-	0	-	-	-	-	-	A	29	38	10	8	-	0.2	-	-	28	27	93	-	-
Semolina																																			
maize.....	11.0	8.8	1.1	-	78.0	-	365			440 ²	0.15	0.05	0.05	0.5	-	-	-	-	-	-	-	A	1	80	4	20	-	1.0	-	-	73	-	-	-	
wheat.....	13.1	10.3	0.8	-	76	-	362			0	0.12	0.04	0.085	1.3	-	-	E 1.8 ⁴	-	-	-	-	A	1	112	17	-	-	1	-	-	87	-	-	-	
Spaghetti, unenriched, dry.....	10.4	12.5	1.2	-	75.2	0.3	369			0	0.09	0.06	-	2.0	-	-	-	-	-	-	-	A	5	-	22	-	-	1.5	-	-	165	-	-	-	
Tapioca, dry.....	12.6	0.6	0.2	-	86.4	0.1	360			0	0	0.1	-	0	-	0	-	-	-	-	-	0	4	20	12	2	0.69	1.0	0.07	12	4	16	-	-	
Wheat germ.....	11.5	26.6	10.9	2.9	46.7	2.5	363			650	2.0	0.68	0.92	4.2	2.2	0	FA 0.31; E 15 ⁴	-	-	-	-	A	2	780	72	336	-	9.4	1.3	1118	-	-	-	70	

* To convert to kJ (kilojoules) multiply the values given by 4.1855.

** Vitamin A activity due to vitamin A + carotenes; 1 IU vitamin A = 0.0006 mg β-carotene.

*** FA = folic acid; E = α-tocopherol unless otherwise stated.

¹ Enriched.

² Based on yellow maize.

³ Unsalted.

⁴ Total tocopherol.

* To convert to kJ (kilojoule) multiply the values given by 4.1855.

** Vitamin A activity due to vitamin A + carotenes; 1 IU vitamin A = 0.0006 mg β-carotene.

*** FA = folic acid; E = α-tocopherol unless otherwise stated.

1 Enriched.

2 Unsalted.

3 Based on yellow maize.

4 Total tocopherol.

Content per 100 grammes edible portion (unless otherwise stated)	Water g	Proteins g	Fats			Carbohydrates g	Calories* kcal	Vitamins							Purine nitrogen mg	Excess acid A	Excess base B	Elements														
			Total g	Poly- unsaturated g	Cholesterol g			B ₁ mg	B ₂ mg	B ₆ mg	Nicotinic acid mg	Pantothenic acid mg	C mg	Other vitamins***																		
Fats, Oils																																
Butter	17.4	0.6	81.0	4	0.28	0.7	716	3300	trace	0.01	trace	0.1	trace	trace	E 2.4; D 40 IU E 26.2; D 8500 IU	-	A	10 ¹	23	16	1	0.04	0.2	0.03	16	9	-	-	-	-	-	
Cod-liver oil	0	0	99.9	-	0.85	0	901	85000	-	0	-	0	-	-	E ~ 19	-	0	0.1	-	-	-	-	-	-	-	-	-	-	-	-	-	
Corn oil	trace	0	99.9	56	0	0	883	-	-	-	-	-	-	-	E ~ 30	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Cottonseed oil	trace	0	99.9	50	0	0	883	-	-	-	-	-	-	-	E 2	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Lard	1.0	trace	99.0	10	0.1	0	901	0	0	0	0	0	0	0	-	-	A	0.3	0.2	1	-	-	0.1	0.02	3	25	4	-	-	-	-	
Margarine, salted	15.5	0.6	81.0	14	-	0.4	720	3300	-	-	-	-	-	-	E 2	-	-	987	23	20	-	-	0	-	16	-	-	-	-	-	-	
Mayonnaise	15.1	1.1	78.9	32.2	-	3.0	718	280	0.02	0.04	-	trace	-	0	-	-	A	702	53	18	2	-	0.5	-	28	-	-	-	-	-	-	
Mustard, brown	78.1	5.9	6.3	-	-	5.3	91	-	-	-	-	-	-	-	-	-	A	1307	130	124	48	-	1.8	-	134	-	-	-	-	-	-	
Olive oil	trace	0	99.9	8	0	0	883	0	0	0	-	0	-	0	E ~ 3	-	0	0.1	trace	0.5	-	-	0.08	0.07	-	-	-	-	-	-	-	
Palm oil	trace	0	99.9	9	0	0	883	-	-	-	-	-	-	-	E 30	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Peanut butter	1.8	27.8	49.4	11.9	0	17.2	581	-	0.13	0.13	0.30	15.7	2.5	0	biotin 0.04; FA 0.06	-	A	607 ⁴	670	63	178	-	2.0	-	407	-	-	-	-	-	-	
Peanut oil	trace	0	99.9	29	0	0	883	-	-	-	-	-	-	-	E 13	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Safflower oil	trace	0	99.9	72	0	0	883	-	-	-	-	-	-	-	E 31	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Soybean oil	trace	0	99.9	60	0	0	883	-	-	-	-	-	-	-	E 18	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Sunflower oil	trace	0	99.9	63	0	0	883	-	-	-	-	-	-	-	E 22	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Vegetable fat	0	0	100	7	-	0	884	-	0	0	0	0	0	0	-	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Dairy products, Eggs																																
Butter. See under 'Fats', above																																
Cheese																																
Camembert	51.3	18.7	22.8	-	-	1.8	287	1010	0.05	0.45	0.25	1.45	0.1-0.9	0	biotin 0.005	-	A	1150 ⁴	109	382	18	-	0.5	0.08	184	-	-	-	-	-	-	
Cheddar	37	25.0	32.2	1	0.10	2.1	398	1310	0.03	0.46	0.07	0.1	0.40	10.0	biotin 0.004; FA 0.016	-	A	700	82	750	43	-	1.0	-	478	-	-	-	-	-	-	
cottage, creamed	78.3	13.6	4.2	trace	0.015	2.9	106	170	0.03	0.25	-	0.1	-	0	-	-	A	229	85	94	-	-	0.3	-	152	-	-	-	-	-	-	
cottage, uncreamed	79.0	17.0	0.3	-	-	2.7	86	10	0.03	0.82	0.01	0.1	-	1	biotin 0.002; FA 0.03	-	A	290	72	90	-	-	0.4	-	175	-	-	-	-	-	-	
cream	51	8.0	37.7	1	0.12	2.1	374	1540	0.02	0.24	-	0.1	-	0	-	-	A	250	74	62	-	-	0.2	-	95	-	-	-	-	-	-	
Parmesan	30.0	36.0	26.0	-	-	2.9	393	1060	0.02	0.73	-	0.2	-	0	-	-	A	755 ⁴	153	1140	50	-	0.4	-	781	251	1110 ⁴	-	-	-	-	-
Roquefort	40.0	21.0	32.0	-	-	1.8	378	800	0.06	0.3-	-	0.4-	0.5-	0	biotin 0.003	-	A	-	-	700	-	-	1	-	0.36	-	-	-	-	-	-	
Swiss (Emmentaler)	34.9	27.4	30.5	-	-	3.4	398	1140	0.05	0.33	0.09	0.1	-	0.5	E 0.35 ² ; D 100 IU	-	A	620 ⁴	100	1180	55	-	0.9	0.13	860	-	-	-	-	-	-	
Cream																																
heavy 30%	64.1	2.2	30.4	0.8	-	2.9	288	1100 ⁵	0.025	0.17	0.035	0.07	-	1	D 40 IU	-	B	38	78	75	-	-	0-0.1	-	63	-	-	-	-	-	-	
Eggs																																
whole, raw	74.0	12.8	11.5	2.3	0.46	0.7	162	1180	0.12	0.34	0.25	0.1	1.6	0	D 200 IU; B ₁₂ 0.002; E 1; K 0.002; biotin 0.02; FA 0.005	-	A	135	138	54	13	0.05	2.3	0.03	205	197	159	-	-	-	-	

* To convert to kJ (kilojoules) multiply the values given by 4.1855.

** Vitamin A activity due to vitamin A + carotenes; 1 IU vitamin A = 0.0006 mg β-carotene.

*** FA = folic acid; E = α-tocopherol unless otherwise stated.

† Unsalted.

² Total tocopherol.

³ Prepared with corn oil.

⁴ Variable, depends on salt content.

⁵ In summer; in winter 500.

* To convert to kJ (kilojoules) multiply the values given by 4.1855.

** Vitamin A activity due to vitamin A + carotenes; 1 IU vitamin A = 0.0006 mg β-carotene.

*** FA = folic acid; E = α-tocopherol unless otherwise stated.

† Unsalted.

2 Total tocopherol.

3 Prepared with corn oil.

4 Variable, depends on salt content.

5 In summer; in winter 500.

Concent per 100 grammes soluble portion (unless otherwise stated)	Fat					Carbohydrates					Vitamins					Minerals																
	g	g	g	g	g	g	g	g	g	g	A ¹⁰ IU	B ₁ mg	B ₂ mg	B ₆ mg	Niacin acid mg	Ascorbic acid mg	C mg	Other vitamins ¹⁰⁰ mg	Purine Nitrogen mg	Essential Amino Acids ¹⁰⁰ mg	Sodium mg	Potassium mg	Calcium mg	Magnesium mg	Iron mg	Copper mg	Zinc mg	Phosphorus mg	Sulphur mg	Chlorine mg		
Egg white, raw	87.6	10.9	0.2	-	0	0.8	51	0	0.02	0.23	0.22	0.1	0.14	0				biotin 0.002, FA 0.001	-	A	192	148	9	13	0.04	0.2	0.03	37	208	161		D Chlorine
Egg yolk, raw	50.0	56.1	33.5	6.7	1.6	0.6	360	34.0	0.32	0.52	0.50	0.02	4.2	0				B ₁₂ 0.002, E 3, D 3.5 IU, biotin 0.05, FA 0.013	-	A	50	123	141	16	0.09	7.2	0.02	569	194	142		
Egg, medium (48 grammes)	31.1	6.1	3.5	1.1	0.22	0.4	77	510	0.06	0.16	0.12	0.04	0.8	0				-	-	A	66	67	26	6	0.02	1.3	0.02	98	55	69		
Egg, white, medium (31 grammes)	27.0	3.1	0.1	-	0	0.3	16	6	0.09	0.07	0.07	0.03	0.04	0				-	-	A	37	46	3	3	0.01	0.06	0.01	5	64	48		
Egg yolk, medium (17 grammes)	23.2	2.8	5.4	1.3	0.22	0.1	47	370	0.05	0.09	0.05	0.02	0.7	0				-	-	A	9	21	23	3	0.01	1.2	0.01	93	32	27		
Egg powder	4.1	47.0	41.2	-	2.14	4.1	592	4460	0.35	1.23	0.08	0.2	7.4	0				D 240 IU	-	A	519	483	190	41	-	8.7	0.18	800	630	592		
Milk (cow's) 2 pasteurized, whole	88.5	3.2	5.7	0.1	0.01	4.6	64	140	0.04	0.15	0.05	0.07	0.33	1				E 0.064, B ₁₂ 0.0006, biotin 0.002, D 0.5-4 IU, FA 0.001	-	B	75	139	333	13	0.002	0.04	0.01	88	29	105		
buttermilk, cultured	91.2	5.3	0.5	-	-	4.0	35	35	0.04	0.18	0.04	0.1	0.36	1				B ₁₂ 0.0003, E 0.05-4, biotin 0.002, FA 0.003	-	B	57	147	109	16	-	0.1	0.02	95	30	100		
condensed (sweetened)	27.1	8.1	8.7	0.2	-	54.3	32.1	35.0	0.1	0.38	0.06	0.2	0.85	1				biotin 0.003, D 3.5 IU	-	B	140	340	262	25	-	0.1	-	206	-	-		
evaporated (unsweetened)	73.8	7.0	7.9	0.2	-	9.7	138	350	0.06	0.36	0.03	0.2	0.85	1				biotin 0.003, FA 0.0007, D 3.5 IU	-	B	100	270	252	25	-	0.2	-	205	-	-		
drunk, whole	30	26.4	27.5	0.7	-	58.2	50.2	1290	0.28	1.2	0.3	0.7	2.7	10				B ₁₂ 0.002, biotin 0.013	-	B	410	1330	909	112	-	0.6	0.16	708	254	784		
skimmed	30	35.9	1.0	-	-	52.0	36.2	30	0.35	1.80	0.4	0.9	3.5	10				B ₁₂ 0.002, biotin 0.016, FA 0.0024	-	B	525	1335	1300	111	-	0.6	-	1016	300	1130		
Breast milk ¹⁰	90.9	3.5	0.07	-	0.003	4.8	24	7	0.038	0.17	0.05	0.1	0.29	2				E 0.034, biotin 0.002	-	B	53	150	123	14	-	0.1	0.003	97	-	100		
Carrot milk ¹⁰	87.7	1.03	4.4	0.3	0.01-0.02	6.9	70	330	0.01	0.04	0.02	0.18	0.24	5				biotin 0.003, FA 0.0001, D 0.4-0.7 IU	-	B	17	50	35	3	trace	0.05	0.05	14	14	36		
Corn's milk ¹⁰	87.1	3.7	4.2	-	-	4.1	69	129	-	-	-	-	-	8				B ₁₂ 0.0001, biotin 0.002, FA 0.0002, D 2 IU	-	B	34	180	129	13	0.006	0.1	0.04	103	18	150		
Cook's milk ¹⁰	86.6	3.8	4.2	-	-	4.8	71	120	0.05	0.12	0.027	0.2	0.35	2				B ₁₂ 0.0003, FA 0.0001	-	B	-	70	100	10	-	-	-	60	-	20		
Mare's milk ¹⁰	91.1	2.1	1.25	-	-	4.3	44	45	0.03	0.02	0.03	0.05	0.30	10				B ₁₂ 0.0003, biotin 0.009, FA 0.0002	-	B	50	190	190	-	-	0.1	-	150	-	140		
Sheep's milk ¹⁰	81.6	5.6	7.5	-	-	4.4	107	200	0.07	0.50	-	0.50	0.35	3				biotin 0.002, E 0.024	-	B	45	129	50	1	-	-	-	53	-	-		
Whey	93.5	0.9	0.3	-	-	4.7	25	5-16	0.04	0.08	0.02	0.07	0.35	1.3				-	-	B	62	190	150	-	-	0.2	-	135	-	-		
Yoghurt ¹⁰	86.1	4.8	3.8	-	-	4.5	71	145	0.045	0.024	0.05	0.18	-	2				-	-	B	-	-	-	-	-	-	-	-	-	-		
Meat, Poultry (see unless otherwise stated)																																
Bacon	20.0	9.1	65.0	8.5	0.22	trace	625	0	0.36	0.11	0.35	1.8	-	0				E 0.4	28	A	1770	225	13	15	-	1.2	-	108	-	-		
Beef, medium fat																																
Values per 100 g	pH	Spec grav	Casein	Albumin	Total protein	Nonprotein N	Ash																									
Beef, milk	6.97	1.031	0.40 g	0.30 g	1.0-6.0 g	32.4 mg	0.21 g																									
Canned milk	6.60	1.031	2.80 g	0.40 g	3.4-3.8 g	40 mg	0.68 g																									
Corn's milk	-	1.031	2.87 g	0.89 g	2.0-6.0 g	40 mg	0.72 g																									
Mare's milk	7.20	1.034	1.40 g	-	3.6-3.8 g	40 mg	0.85 g																									
Sheep's milk	6.54	1.036	4.17 g	0.98 g	2.1-3 g	42.5 mg	0.36 g																									

* To convert to I.U. (fat-soluble) multiply the values given by 4.1855

** Vitamin A activity due to vitamin A + carotenes, 1 IU vitamin A = 0.0006 mg β-carotene

*** FA = folic acid; E = ascorbic acid unless otherwise stated.

† See also pages 687-689

‡ Can be calculated from the 100 g values.

§ Total ascorbic acid.

¶ Citric acid 232 mg, lactic acid 487 mg, succinic acid 44 mg

Content per 100 grammes edible portion (unless otherwise stated)	Water	Proteins	Fats			Carbohydrates	Calories*	Vitamins						Purine nitrogen	Excess acid A	Excess base B	Elements																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
			Total	Poly-unsaturated	Cholesterol			A** IU	B ₁ mg	B ₂ mg	B ₆ mg	Nicotinic acid mg	Pantothenic acid mg				C mg	Other vitamins***	Sodium mg	Potassium mg	Calcium mg	Magnesium mg	Manganese mg	Iron mg	Copper mg	Phosphorus mg	Sulphur mg	Chlorine mg																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																													
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* To convert to kJ (kilojoule) multiply the values given by 4.1855.

** Vitamin A activity due to vitamin A + carotenes; 1 IU vitamin A = 0.0006 mg β-carotene.

*** FA = folic acid; E = α-tocopherol unless otherwise stated.

† Total tocopherol.

Tanderil®
Geigy



brings
inflammation
under control

Content per 100 grammes edible portion (unless otherwise stated)	Water g	Proteins g	Fats			Carbohydrates g	Calories* kcal	Vitamins							Purine nitrogen mg	Excess acid A	Excess base B	Elements																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																												
			Total g	Poly- unsaturated g	Cholesterol g			A** IU	B ₁ mg	B ₂ mg	B ₆ mg	Nicotinic acid mg	Pantothenic acid mg	C mg				Other vitamins*** mg																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																												
Sausages (continued)																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																														

* To convert to kJ (Kilojoules) multiply the value in kcal by 4.184

Concent per 100 grammes edible portion (unless otherwise stated)	Fats				Vitamins										Elements																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																							
	Water	Protein	Total	Poly- unsaturated	Cholesterol	Carbohydrates	Calorics [†]	A** IU	B ₁ mg	B ₂ mg	B ₆ mg	Nicotinic acid mg	Pantothenic acid mg	C mg	Other vitamins***	Fatty acids A Lactic acid B	Elements																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																					
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Herring (<i>Clupea harengus</i>)	62.8	17.3	18.8	-	-	0	243	130	0.06	0.24	0.45	4.3	1.0	0.5	E 2 ⁺ , B ₁₂ 0.01, D 500 IU [†]	119	A	118	317	57	26	0.02	1.1	0.3	240	202	122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

* To convert to IU (kilocalorie) multiply the values given by 4.1855

** Vitamin A activity due to vitamin A + carotenoids. 1 IU vitamin A = 0.0006 mg β -carotene*** 1 A = folic acid, E = α -tocopherol unless otherwise stated.

† Without gonads

‡ Total tocopherol

Amino acids of foods

The amino-acid contents of foods listed in the table below have been taken from a publication¹ of the British Medical Research Council. Other collected data on the subject are available in the publications of BLOCK and BOLLING², BLOCK and WEISS³, ORR and WATT⁴, and HARVEY⁵. The amounts of the essential amino acids in foods are given in the tables of SOUCI et al.⁶ and of CHURCH and CHURCH⁷. The amino-acid content of the FAO/WHO Reference Protein⁸ is based on the minimum requirements of the individual essential amino acids.

Many of the proteins of meat and fish have a largely similar composition, like those of cereal and milk products, and it has therefore been unnecessary to list all these foods in detail. On the other hand, the amino-acid composition of the vegetable proteins shows wide variations, but since these proteins are quantitatively unimportant in the human diet the variations are without appreciable effect in nutrition. Too little is known of the amino-acid composition of fruits to justify their inclusion in the table. The phenylalanine content of fruits lies between 1.5 and 4 g/16 g N⁹.

Amino-acid contents of foods (g per 16 g nitrogen*)

	Arginine	Cystine	Histidine	Isoleucine	Leucine	Lysine	Methionine	Phenylalanine	Threonine	Tryptophan	Tyrosine	Valine	Alanine	Aspartic acid	Glutamic acid	Glycine	Proline
<i>Vegetables</i>																	
Beans, snap	5.9	1.1	2.9	5.4	7.7	5.4	0.5	3.4	2.6	1.0	3.0	5.1	2.6	6.6	1.4	3.7	4.
haricot	5.8	1.0	3.2	6.1	8.2	7.0	1.3	6.2	4.6	1.3	—	6.6	—	—	—	—	—
Beets	1.8	—	1.4	3.2	3.4	3.4	0.5	1.4	2.4	1.0	—	3.0	—	—	—	—	—
Beets, tops	6.1	1.4	1.9	3.2	6.2	3.5	2.4	5.0	4.2	1.4	4.5	5.1	—	—	—	—	—
Broccoli	5.8	—	1.8	3.8	5.3	5.4	1.8	3.0	3.4	1.3	—	4.2	—	—	—	—	—
Brussels sprouts	6.2	—	2.2	4.2	4.3	4.3	1.0	3.4	3.4	1.0	—	4.3	—	—	—	—	—
Cabbage	7.5	1.6	1.8	2.9	4.2	3.7	1.0	2.6	2.7	0.8	2.1	3.4	—	—	—	—	—
Carrots	3.5	—	1.4	4.3	5.8	4.5	1.1	3.7	3.8	0.8	—	5.4	—	—	—	—	—
Cauliflower	4.2	—	0.2	4.3	6.2	5.4	2.1	3.4	4.2	1.3	—	5.8	—	—	—	—	—
Lentils	8.3	0.6	2.2	5.3	7.0	6.2	0.6	4.2	3.7	0.8	—	5.6	—	—	—	—	—
Peas	8.6	1.0	1.8	5.0	6.9	5.3	1.0	4.0	4.0	1.0	4.2	4.6	(3.8)	(8.6)	(3.2)	(6.1)	—
Potatoes	5.3	1.3	1.4	4.5	4.6	5.0	1.6	4.2	3.7	1.3	2.9	5.1	4.2	17.1	23.8	1.9	2.6
Spinach	4.5	—	1.4	4.0	6.4	5.1	1.8	4.5	4.0	1.8	—	5.1	—	—	—	—	—
Soybeans, soyflour ..	7.4	1.9	2.6	5.3	7.7	6.4	1.3	5.0	4.0	1.4	3.7	5.3	5.0	1.3	19.0	4.5	5.3
<i>Nuts</i>																	
Almonds	10.1	1.8	2.2	3.8	6.6	2.6	1.3	5.1	2.7	0.8	—	5.0	—	—	—	—	—
Brazil nuts	13.3	3.0	2.1	3.7	6.9	2.6	5.1	3.4	2.6	1.1	—	4.8	—	—	—	—	—
Coconuts	12.5	1.8	2.1	4.5	7.2	3.5	1.8	4.2	3.0	2.1	—	5.6	—	—	—	—	—
Hazelnuts	14.6	2.6	1.9	5.8	6.2	2.9	1.0	3.7	2.9	1.4	3.7	6.2	—	7.0	20.5	9.4	5.6
Peanuts	10.6	1.6	2.4	4.2	6.2	3.5	1.0	5.0	2.9	1.1	3.0	5.0	2.9	14.1	2.0	5.4	5.1
Walnuts	13.0	1.8	2.2	4.3	6.9	2.6	1.8	4.3	3.4	1.0	—	5.4	—	—	—	—	—
<i>Cereals</i>																	
Barley, whole grain ..	5.0	2.1	1.9	3.8	6.9	3.4 ¹	1.4	5.0	3.7	1.4	3.5	5.0	4.5	5.9	20.5	43.2	9.3
Bread, wheat, white ..	3.4	2.2	2.1	3.7	7.4	1.9	1.9	5.0	2.9	—	3.2	4.2	3.0	4.2	33.0	3.4	11.5
Flour, wheat, whole ..	4.3	2.1	2.1	3.8	6.4	2.7	1.6	4.6	2.9	1.3	3.2	4.3	3.4	5.0	27.7	3.8	10.1
white	3.4	2.2	2.1	3.7	7.0	1.9	1.6	5.4	2.9	1.3	3.4	4.2	3.2	4.2	33.4	3.4	11.7
Maize, whole grain ..	5.0	2.1	2.4	4.0	12.0	3.0	2.1	5.0	4.2	0.8	3.8	5.6	9.9	12.3	15.4	3.0	8.3
Oats, whole grain ...	6.6	1.8	1.9	4.6	7.0	3.7	1.4	5.0	3.4	1.3	3.8	5.4	5.1	4.2	18.4	4.2	5.8
Rice, whole	8.5	1.8	2.2	4.8	8.2	4.2	2.1	4.6	3.5	1.4	5.8	6.2	—	—	—	—	—
polished	8.0	1.6	2.2	4.6	8.5	3.0	2.1	4.8	3.8	1.4	5.0	6.6	5.6	4.5	10.7	6.6	4.5
Rye, whole grain ...	5.0	1.8	2.1	3.8	6.1	3.7	1.6	4.6	3.4	1.3	4.2	5.0	—	—	19.7	—	—
Wheat germ	6.9	1.4	2.7	3.5	5.9	6.1	1.4	3.7	4.5	1.0	—	4.6	—	—	—	—	—
<i>Eggs, Milk</i>																	
Eggs, whole	6.4	2.1	2.6	5.8	9.0	6.7	3.0	5.3	5.3	1.8	4.3	7.2	—	10.7	12.3	3.8	4.3
Egg white	6.2	2.2	2.4	5.8	9.0	6.6	4.0	5.9	5.0	1.9	4.2	7.8	—	11.0	12.6	4.2	4.2
Egg yolk	7.0	1.8	2.6	5.8	8.5	6.7	2.2	4.6	5.8	1.8	4.6	6.9	—	—	12.0	3.4	4.3
Milk, cow's, and dairy products ...	3.7	0.8 ²	2.7	6.2	9.9	7.8	2.4	5.1	4.6	1.4	5.6	7.0	3.7	8.2	22.2	1.9	9.8
Breast milk	3.4	1.9	2.2	5.6	9.4	6.2	2.1	4.0	4.5	1.6	4.8	6.2	3.8	9.3	19.8	2.2	8.6
<i>Meat, Fish</i>																	
Fish	5.8 ³	11.2	2.1 ⁴	5.1	7.5	9.0	2.9	3.7	4.5	1.0	3.0	5.3	6.1	9.4	14.1	6.1	5.9
Gelatin	7.8	trace	6.9	1.4	2.9	4.0	0.8	2.1	1.9	—	0.3	2.2	9.8	5.9	10.1	24.2	26.7 ⁵
Meat and meat products ...	6.6	1.3	3.2	5.1	7.8	8.2	2.4	4.2	4.5	1.3	3.4	5.3	6.2	9.1	15.4	4.5	4.2
brain, liver, kidney	6.1	1.3	3.2	5.1	9.0	8.2	2.4	5.1	4.5	1.3	3.4	6.1	6.2	9.1	15.4	4.5	4.2
<i>FAO/WHO Reference Protein...</i>	—	—	—	4.3	4.9	4.3	2.3	2.9	2.8	1.4	2.9	4.3	—	—	—	—	—

* Average nitrogen content per 100 g protein. ¹ Barley, pearled 2.2. ² Cheese 0.5. ³ Shrimps 9.4. ⁴ Mackerel 3.7; tunny 5.8. ⁵ Including hydroxyproline

The values in the table are for the raw foods. Cooking little effect on the proteins of foods poor in carbohydrate products the proteins in the crust have a lower utilization known that vegetables lose nitrogenous substances during, but this loss has no practical significance.

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ponent parts of the body changes with age, and the parts do all mature chemically at the same rate. The composition of the whole body at any age is the resultant of the composition of its ues and of their contribution to the weight of the body at that

Methods of determining the composition of the whole body

There are two main methods of determining the composition of the whole body. The first is by direct measurement of the body as a whole, and the second is by indirect measurement of the composition of the tissues and organs and tissue than about that of the body as a whole.

Dilution methods depend upon introducing into the body a

known substance, the volume of fluid in which the substance has become distributed can be calculated. By the use of appropriate substances it is possible to estimate the amounts of total water, of extracellular fluid, and of intracellular fluid in the body.

The choice of substance depends upon the nature of the substance used, and the use of each involves certain assumptions (for discussion of these see the literature*)

According to the substance used, and the use of each involves certain assumptions (for discussion of these see the literature*)

* This chapter on the 'Composition of the Body' (pages 517-522) has been compiled by E. M. WIDDOWSON and J. W. T. DICKINSON, Department of Experimental Medicine, University of Cambridge, England.

amount of any mineral in the body but only that fraction of it which is 'exchangeable'.

Determination of the composition of the tissues

The composition of the tissues is determined by direct measurement of the tissues and organs and tissue than about that of the body as a whole.

Changes in composition during development

The proportion of fat in the human body increases rapidly during the last 2 months of gestation and the full-term baby has about 16%.

The proportion of water in the body increases rapidly during the last 2 months of gestation and the full-term baby has about 75%.

There is a decrease in the proportion of water in the fat-free body tissue and an increase in that of solid matter. The fall in the proportion of total water is due to the large reduction in the amount of extracellular fluid that accompanies growth; this exceeds the small rise in the amount of water inside the cells due to the increase in the

proportion of fat in the body. The proportion of solid matter in the body increases during postnatal life.

The proportion of calcium in the body increases during postnatal life.

The skeleton and the proportion of calcium in the body more than doubles during postnatal life.

References

Widdowson, E. M., and Dickinson, J. W. T. (1954). *Mineral Metabolism*, vol. 2, part A, Academic Press, New York, 1964, page 1.

Composition of the whole body as determined by chemical analysis (values per kilogramme fat-free tissue unless otherwise stated)

	Body weight kg	Water* g	Fat* g	Water g	N g	Na mEq	K mEq	Cl mEq	Mg g	Ca g	P g	Fe mg	Cu mg	Zn mg	B mg	Co mg
Foetus	0.02	898	2	900	10.5	110	48	80	0.10	2.1	2.1	-	-	-	-	-
Foetus	0.20	876	5	880	13.0	102	42	76	0.14	3.5	2.5	54	3.3	20	-	-
Foetus	1.0	851	10	860	18.4	94	42	68	0.20	6.3	3.9	65	3.4	20	-	-
Foetus	2.0	790	60	840	21.0	88	45	62	0.24	7.8	4.8	84	4.0	20	-	-
Newborn, full-term	3.5	687	160	820	22.6	82	53	55	0.26	9.6	5.6	94	4.7	20	-	-
Adults	70	605	160	720	34.0	80	69	50	0.47	22.4	12.0	74	1.7	28	0.37	0.02

* Per kilogramme whole body weight

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Composition of the whole body as determined by dilution methods

	Total water as percentage of body weight	Extracellular fluid as percentage of body weight	Exchangeable		
			Na	K	Cl
			mEq/kg body weight	mEq/kg body weight	mEq/kg body weight
Newborn, 1-27 hours ¹	-	-	-	35.5	-
Newborn, 1 day ²	79.0 (deuterium oxide)	43.9 (thiosulphate)	-	-	-
Infants, 2-4 weeks ³	-	-	-	-	48.1
Infants, 2 weeks-2 months ⁴	-	-	76.4	-	-
Men ⁵	59.1 (deuterium oxide)	15.6 (inulin)	41.7	48.1	31.9
	59.6 (tritium oxide)	16.3 (thiosulphate)	-	-	-
	53.4 (antipyrine)	22.9 (thiocyanate)	-	-	-
	60.2 (urea)	-	-	-	-
Women ⁵	51.0 (deuterium oxide)	16.0 (thiosulphate)	40.5	38.2	28.6
	43.4 (antipyrine)	20.9 (thiocyanate)	-	-	-
	57.0 (urea)	-	-	-	-

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Composition of muscular tissues (values per kilogramme fat-free tissue)

		Weight as percentage of body weight	Water g	N g	Na mEq	K mEq	Cl mEq	Mg mEq	Ca mEq	l mn
Skeletal muscle ¹	Foetus, 14 weeks	-	907	11.5	101	56.3	76.4	11.7	5.6	36
	Foetus, 20-22 weeks ..	25	887	15.4	90.6	57.6	65.6	10.5	7.1	40
	Newborn	25	804	20.9	60.1	57.7	42.6	14.8	4.3	47
	Infants, 4-7 months ..	-	785	29.6	50.1	89.5	35.5	20.0	3.1	64
	Adults	43	792	31.4	36.3	92.2	22.1	16.7	2.8	58
Heart ² Whole	Foetus, 20 weeks	0.6	860	14.0	46.1	81.1	41.0	-	-	49.
	Newborn	0.5	841	19.6	64.2	54.3	45.2	10.9	7.4	47.
	Infants, 4-7 months ..	-	830	21.0	59.8	49.3	49.3	11.0	8.2	49.
	Adults	0.4	827	22.9	57.8	66.5	45.6	13.2	2.6	49.
	Adults	-	789	-	44.7	78.5	38.0	17.0	3.9	63.
Left ventricle	Adults	-	789	-	44.7	78.5	38.0	17.0	3.9	63.
Right ventricle	Adults	-	802	-	47.8	56.2	39.5	16.5	3.8	50.
Auricles	Adults	-	812	-	52.2	35.7	42.2	-	-	30.
Septum	Adults	-	792	-	40.5	79.0	33.8	-	-	51.
Myometrium ³	Non-pregnant	-	794	-	87.8	62.6	73.8	12.8	16.6	-
	Early pregnant	-	825	-	93.6	59.0	71.0	8.5	7.1	-
	At term	-	823	-	88.8	62.4	63.2	13.5	17.5	-

References

¹ DICKERSON and WIDDOWSON, *Biochem. J.*, 74, 247 (1960).² WILKINS and CULLEN, *J. clin. Invest.*, 12, 1063 (1933); MANGUN et al., *Arch. intern. Med.*, 67, 320 (1941); ALEXANDER et al., *J. Lab. clin. Med.*, 36,796 (1950); CLARKE and MOSHER, *Circulation*, 5, 907 (1952); WIDDOWSON and DICKERSON, *Biochem. J.*, 77, 30 (1960).³ HAWKINS and NIXON, *J. Obstet. Gynaec. Brit. Emp.*, 65, 895 (1958).

Organic composition of the adult brain and spinal cord (values per kilogramme fresh tissue unless otherwise stated)¹

	Whole brain g	Grey matter g	White matter g	Spinal cord g
Total phospholipid P	250*	30.8	78.2	51-
Lecithin P	-	7.9-13.2	9-15	22†
Cephalin P	148-260*	18-22	27-35	61†
Diphosphoinositide P	-	1.96	4.14	-
Sphingomyelin P	-	2.7	10.8	-
Cerebrosides	-	6.3 ± 2.9	49.0**	12.9-
		3.1 ± 0.2**		6†
Total lipids	104	57.9	179	-
Cholesterol	26-44	7.2	40.7	55
Gangliosides (N-acetylsialic acid × 4.0)	-	3.3	1.25	-
Total protein	100-110	73-82	77-92	90
Soluble in 4.5% KCl (isoelectric point pH 5.6)	-	16.7-18.9	18.5-22.1	-
Soluble in water (isoelectric point pH 4.6)	-	21.9-24.6	14.6-17.5	-
Proteolipid protein ²	-	16	42	-
Neurokeratin	-	3.1	11.2	-

* Values per kilogramme dry weight.
 ** 'True' cerebrosides.
 † Not expressed as P.
 ‡ White matter.

References
¹ (Except proteolipid protein) ANSELL, G.B., in LONG, C. (Ed.), *Biochemical Handbook*, Spon, London, 1961, page 640.
² Approximate values calculated from FOLCH and LEES, *J. Biol. Chem.* 807 (1951).

Composition of skin, hair and nails (values per kilogramme fresh weight unless otherwise stated)

		Weight as percentage of body weight	Water g	N g	Na mEq	K mEq	Cl mEq	Mg mEq	Ca mEq	P mmol	Cu mg	Fe mg	Mn** mg	Pb mg	
Skin ¹	Foetus, 14 weeks	-	917	11.6	-	23.8	90.6	-	4.4	41.8	-	-	-	-	
	Foetus, 20 weeks	13	901	11.9	120	36.0	96.0	3.8	6.1	28.2	-	-	-	-	
	Newborn	15	828	26.5	87.1	45.0	66.9	4.7	10.0	31.7	-	-	-	-	
	Infants, 3-5 months	-	675	54.5	65.4	43.7	72.3	7.4	11.4	34.9	-	-	-	-	
	Adults	7	694	53.0	79.3	23.7	71.4	3.1	9.5	14.0	-	-	-	-	
Epi- dermis ²	Adults	-	645	-	49.6	81.4	-	15.0	7.5	-	-	-	-	-	
Hair* ³	Adults	-	-	-	-	-	-	0.8-8.4	94-245	-	4-128	0.8-170	0.00001-46	17-508	150
Nails* ⁴	Adults	-	-	-	-	-	-	1.9-9.2	-	-	9-81	18-65	< 1	97-240	170

* Hair and nails also contain Zn (9-562 and 116-3080 mg/kg respectively). The presence in hair of Al, Ni, Co and Cr together with traces of Ti, Sr and Ag has also been reported.
 ** Values per kilogramme dry weight.

References

- ¹ WIDDOWSON and DICKERSON, *Biochem. J.*, **77**, 30 (1960).
² SUNTZEFF and CARRUTHERS, *J. Biol. Chem.*, **160**, 567 (1945); ZHEI and FOX, *Arch. Derm.*, **61**, 397 (1950).
³ FOLCH and LEES, *J. Biol. Chem.*, **187**, 247 (1950).
⁴ CARRUTHERS, *Chemical Analysis of the Human Body*, University of Chicago Press, Chicago, 1954, page 662.

Composition of teeth and bones (values per 100 gramme dry fat-free tissue unless otherwise stated)

		Water ^a	N	Ca	P	Mg	CO ₂	Cl	F	Na	K	Fe	Cu	Pb
		g	g	g	g	g	g	g	g	g	g	g	g	g
Teeth ¹	Enamel	Adults ...	3	0.03	36	17	0.4	2.5	0.010-0.034	0.71-0.90	0.05-0.30	0.0008-0.4	0.00017-0.0009	-
	Dentine	Adults	10	3.4	27	13	0.9	3.3	0.00-0.03	0.024-0.076	0.30-0.07-0.10	0.007	-	0.005
<i>Bone tissue²</i>														
Cortex of femur	Foetus, 14 weeks	-	5.95	18.9	9.1	-	-	-	-	-	-	-	-	-
	Foetus, 20-24 weeks	31.3	5.25	23.4	10.5	-	-	-	-	-	-	-	-	-
	New born	23.8	5.06	24.6	10.8	-	-	-	-	-	-	-	-	-
	Infants, 2-4½ months	23.0	5.28	23.7	10.8	-	-	-	0.049**	-	-	-	-	-
	Infants, 5-9 months	19.5	5.31	24.9	11.0	-	-	-	-	-	-	-	-	-
	Infants, 12-24 months	20.3	5.24	24.6	11.1	-	-	-	0.071**	-	-	-	-	-
	Children, 12 years	15.5	4.92	25.3	11.5	-	-	-	-	-	-	-	-	-
	Adults, 18-35 years	12.2	4.74	26.4	11.3	0.39	4.0	0.18	0.094-0.270**	0.18-0.6	0.05-0.3	0.011-0.017	0.0002-0.0048	0.001-0.01
	Whole femur (excluding epiphyses)	Foetus, 14 weeks	56.0	5.69	15.8	7.1	-	-	-	-	-	-	-	-
	Foetus, 20-24 weeks	54.6	5.95	19.1	8.2	-	-	-	-	-	-	-	-	-
	New born	48.8	5.94	23.6	9.9	-	-	-	-	-	-	-	-	-
	Infants, 2-4½ months	49.2	6.78	19.9	9.7	-	-	-	-	-	-	-	-	-
	Infants, 5-9 months	45.7	6.89	19.0	8.6	-	-	-	-	-	-	-	-	-
	Infants, 12-24 months	39.7	5.67	18.3	8.5	-	-	-	-	-	-	-	-	-
	Children, 12 years	30.7	5.21	27.2	12.4	-	-	-	-	-	-	-	-	-
	Adults, 18-35 years	22.7	5.20	25.1	10.7	-	-	-	-	-	-	-	-	-

^a Per 100 gramme fat free bone** Increases with age and with the amount in the drinking water. Values given are for ribs (JACKSON and WILDMANN *J Path Bact*, 76, 451 (1958))

References

¹ EASTOE, J. E., in LONG, C. (Ed.), *Biochemistry's Handbook*, Spon, London, 1961, page 720² EASTOE, J. E., in LONG, C. (Ed.), *Biochemistry's Handbook*, Spon, London, 1961, page 715; DISKESON, J. W. T., *Biochem J*, 82, 56 (1962)

Strontium and barium contents of ashed bone (μg/g)

Age	Sr	Ba
0-3 months	79.1	7.0
1-13 years	73.8	7.6
19-33 years	107	5.1
33-74 years	114	8.5

Reference

SOMMER and STRECH *Biochem J*, 47, 104 (1957)Strontium-90: calcium ratio in bone (pCi ⁹⁰Sr/g Ca)

Age	Mean	Maximum
0-5 years	2	3.2
5-20 years	1	2.0
Over 20 years	0.3	0.6

Reference

SCHUBERTSCH, W., *Z Ernährungswiss*, 2, 123 (1962) Values from Western Germany 1960

Composition of the Body

Organic components of soft and hard tissues (values per kilogramme fresh tissue unless otherwise stated)

		Non-protein N g	Sarcoplasmic protein N g	Fibrillar protein N g	Collagen N g	Glycogen g	Mucopolysaccharides g	Cholesterol g
Skeletal muscle ¹	Foetus, 14 weeks	1.2	3.6	5.7	0.6	-	-	-
	Foetus, 20-22 weeks	1.7	3.7	8.7	1.8	-	-	-
	Newborn	2.4	3.9	10.9	3.8	-	-	-
	Infants, 4-7 months	3.2	5.0	17.0	4.6	-	-	-
	Adults	3.0	6.7	19.9	1.4	-	-	2.7 ²
Uterus ²								
Muscle	Non-pregnant	-	-	5, 11, 4*	-	-	-	10**
	Pregnant, at term	-	-	13, 9, 15*	-	-	-	-
Mucous membrane	Proliferative phase	-	-	-	-	3.2	-	-
	Early differentiation phase	-	-	-	-	11.2	-	-
	Secretory phase	-	-	-	-	6.4	-	-
Skin ³	Foetus, 20-22 weeks	-	-	-	2.4	-	-	-
	Newborn	-	-	-	16.8	-	2.9†	-
	Infants, 4-7 months	-	-	-	39.2	-	-	-
	Adults	-	-	-	45.7	-	2.0†	-
Bone ⁴	Foetus, 14 weeks	-	-	-	29.2†	-	-	-
	Foetus, 20-24 weeks	-	-	-	40.6†	-	-	-
	Newborn	-	-	-	42.0†	-	-	-
	Infants, 2-4½ months . .	-	-	-	44.0†	-	-	-
	Infants, 5-9 months	-	-	-	42.7†	-	-	-
	Infants, 12-24 months . .	-	-	-	43.7†	-	2.3††	-
	Adults, 18-35 years	-	-	-	41.5†	-	1.6††	-
Teeth ⁵								
Enamel	Adults	-	-	-	0.16**	-	1.0 (Soluble enamel protein)	-
Dentine	Adults	-	-	-	30.6-32.4**	-	2.0-6.0	4.0

* Values for actomyosin, myosin and actotropomyosin respectively.

** Per kilogramme dry tissue.

† Per kilogramme dry fat-free tissue.

†† Per kilogramme dry weight as glucosamine hydrochloride.

References

¹ DICKERSON and WIDDOWSON. *Biochem. J.*, **74**, 247 (1960).

² CSAPO, A., *Amer. J. Physiol.*, **160**, 46 (1950); NAESLUND and SNELLMAN, *Acta Soc. Med. upsalien.*, **59**, 349 (1954); ARRONET and LATOUR, *J. clin. Endocr.*, **17**, 261 (1957).

³ WIDDOOWSON and DICKERSON, *Biochem. J.*, **77**, 30 (1960); LOEWI, G., *Biochim. biophys. Acta*, **52**, 435 (1961).

⁴ ROGERS, H. J., *Nature*, **164**, 625 (1949); DICKERSON, J. W. T., *Biochem. J.*, **82**, 56 (1962).

⁵ EASTOE, J. E., in LONG, C., (Ed.), *Biochemists' Handbook*, Spon, London, 1961, page 720.

Composition of placenta and amniotic fluid (values per kilogramme fresh placenta and per litre amniotic fluid)

	Stage of gestation	Water g	N g	Na mEq	K mEq	Cl mEq	Mg mEq	Ca mEq	P mmol	Cu mg	Zn mg
Placenta ¹	20-40 weeks	866	18.5	98	40	-	6.6	12.4	30	1.5	10.0
Amniotic fluid ²	First half	-	-	135	4.0	109	1.4	3.6	1.2	-	-
	Term	-	-	-	-	-	-	-	0.7	-	-

References

¹ WIDDOWSON and SPRAY, *Arch. Dis. Childh.*, 26, 205 (1951); for further values see BERGER and VON HORNSTEIN, *Fortschr. Geburtsh. Gynäk.*, 14, 1 (1961).

² MAKEPEACE et al., *Surg. Gynec. Obstet.*, 53, 635 (1931); ECONOMOU-MAVROU and McCANCE, *Biochem. J.*, 68, 573 (1958); WESTIN et al., *Acta paediat. (Uppsala)*, 49, 154 (1960).

his chapter on 'Water and Electrolyte Balance' has been compiled by U. F. GAUGER and M. ALLODWIN of the University Surgical Unit, Basle. It should be read in conjunction with the chapter on 'Ureous Solutions', pages 270-271.

The treatment of water and electrolyte disturbances is a matter entering a balance. In healthy adults the total intake of each nutrient is equal to its total excretion. Treatment thus calls for a wedge of the daily water, electrolyte and caloric requirements be adult and of the ways and amounts in which they are excreted. patients it is necessary to take into account not only the daily rakes but also the amounts of water and electrolytes which have in and are being excreted. The success of treatment is therefore dependent on precise determination of the total intake (food, drink,

for standardized conditions. It is essential to rectify the whole electrolyte and water balance of the patient, the mere correction of individual abnormal plasma concentrations does not suffice.

Composition of the body

This is shown in detail in the chapter 'Composition of the Body' pages 517-522.

Table 1 Approximate composition of the whole body and distribution of the body water expressed as percentage of the body weight

	Adults		Infants
	Men	Women	
Solids	40	50	25
Organic substances	35	45	-
Minerals	5	5	-
Total body water	60	50	75
Intracellular	40	30	40
Extracellular	20	20	35
(a) Intravascular	4	4	5
(b) Interstitial	16	16	30

Electrolyte composition of the body fluids

For a more detailed discussion of the serum electrolyte composition see under 'Blood', page 561 sq.

Table 2 Concentrations of the principal electrolytes in serum, serum water and the interstitial and intracellular fluids*

	Serum		Serum water	Interstitial fluid*	Intracellular fluid**
	mEq/l	mg/l	mEq/l	mEq/l	mEq/kg water
Cations					
Sodium	142	3265	152.7	145	10
Potassium	4	156	4.3	4	160
Calcium	5	100	5.4	5	2
Magnesium	2	24	2.2	2	26
Cations, total	153	3545	164.6	156	198
Anions					
Chloride	101	3581	108.5	114	3
Bicarbonate	27	1648	29.3	31	10
Phosphate (HPO_4)	2	96	2.2	2	100
Sulphate	1	48	1	1	20
Organic acids	6	210	6.4	7	-
Proteins	16	66300	17.2	1	65
Anions, total	153	71900	164.6	156	198

Table 3 Conversion factors for serum electrolytes (see also page 276)

	Serum concentrations				Conversion factors			
	mEq/l	mmol/l	meq/l	mg/l	mg/l to mEq/l	mg/100 ml to mEq/l	mEq/l to mg/l	mEq/l to mg/100 ml
Cations								
Sodium	142	142	142	3265	0.0435	0.435	23.0	2.30
Potassium	4	4	4	156	0.0256	0.256	39.1	3.91
Calcium	5	2.5	2.5	100	0.0499	0.499	20.0	2.00
Magnesium	2	1	1	24	0.0823	0.823	12.2	1.22
Cations, total	153	149.5	149.5	3545	-	-	-	-
Anions								
Chloride	101	101	101	3581	0.0282	0.282	35.5	3.55
Bicarbonate	27	27	27	1648	0.0164*	0.164*	61.0*	6.10*
Phosphate (HPO_4)	2	1	1	96	0.0208	0.208	49.0	4.90
Sulphate	1	0.5	0.5	48	0.0208	0.208	49.0	4.90
Organic acids	6	6	6	210	0.0286	0.286	35	3.5
Proteins	16	2	2	66300	0.000241**	0.00241**	4145**	414.5**
Anions, total	153	137.5	137.5	71900	-	-	-	-
Total cations + total anions	306	287	287	75400	-	-	-	-

* For the conversion of mEq/l to mmol/l and vice versa see page 276.

** The VAN SLYKE factor of 2.41 for the conversion of serum protein (g/100 ml) into ionized serum protein (mEq/l) is valid for 38°C, pH 7.4 and an albumin/globulin ratio of 1.6. When the distribution of the plasma protein

fraction is abnormal, new serum protein calculation of the equivalent value for the albumin and globulin by means of the following formula: Ig albumin nitrogen = 1.745 mEq/l, Ig globulin nitrogen = 1.205 mEq/l. According to BROUWER these factors give values that are too high.

Water balance

Table 4 Average daily water turnover of an adult weighing 70 kg⁴

	Water intake (g)			Water output (g)	
	Obligatory	Facultative		Obligatory	Facultative
Drink	650	} 1000	Urine	700	} 1000
Food	750		Skin	500	
Oxidative ..	350		Lungs	400	
			Faeces	150	
Subtotal ...	1750	1000	Subtotal ...	1750	1000
Total	2750		Total	2750	

Table 5 Daily water requirements in millilitres per kilogramme body weight at various ages under normal conditions^{5, 6}

Age	Body weight kg	Estimated water requirement ml/kg
3 days	3.0	80-100*
10 days	3.2	125-150*
3 months	5.4	140-160
6 months	7.3	130-155
9 months	8.6	125-145
1 year	9.5	120-135
2 years	11.8	115-125
4 years	16.2	100-110
6 years	20.0	90-100
10 years	28.7	70-85
14 years	45.0	50-60
18 years	54.0	40-50
Adults ⁷	70.0	21-43

* Average value for breast-fed infants.

In adults, the daily water, electrolyte and calorie requirements can be calculated with sufficient accuracy from the body weight. In spite of the greater accuracy of values derived from body surface area this method offers no advantage since the actual requirements are also subject to other factors like age, sex, the functional state of the heart, kidneys and lungs, fever, disease, nutritional status and calorie consumption. In newborn as well as older children, however, the requirements should be calculated from the body surface area (see the nomogram on page 538) or the daily calorie turnover.

Table 6 Daily water requirements per square metre body surface area⁶

Minimum requirement	870 ml/m ²
Average requirement	1500 ml/m ²
Maximum tolerance	2730 ml/m ²

Table 7 Average daily water turnover per 100 kcal¹

Water intake	80-110 ml/100
Water of oxidation	10-20 ml/100
Urine	50-70 ml/100
Insensible water loss (see also Table 8) ..	40-60 ml/100

Table 8 Average daily insensible water loss at different age

Age	ml/m ²	ml/100
0-3 years	1150	50
3-8 years	950	40
8-16 years	700	40
Adults	550	40

At body temperatures above normal the insensible water loss increases by about 13% for each degree Centigrade⁸ (7% for each degree Fahrenheit). For the water loss by sweating see page 6. In resting infants under 12 months the pulmonary water loss amounts to about 1 g/kg body weight per hour⁵.

With normal bodily activity 25% of the total heat loss of the body is accounted for by evaporation of water (insensible water loss)⁹. The heat of evaporation of water is 0.58 kcal/ml (or 1.7 ml) at 37°C, whence the water loss by evaporation can be calculated from the total calorie expenditure.

Table 9 Water of oxidation¹

Metabolic breakdown of	gives rise to
100 g fat	107 ml water of oxidation
100 g protein	41 ml water of oxidation
100 g carbohydrate	55 ml water of oxidation
100 g nonfatty tissue	15 ml water of oxidation

That the proteins of nonfatty tissue are not fully oxidized is shown by the presence of a nonoxidized C-atom in the urea excreted in the urine. The breakdown of nonfatty tissue not only gives rise to water of oxidation but also releases the intracellular water (about 100 g). Fatty tissue contains practically no water¹⁰.

Table 10 Water arising from metabolic breakdown of body tissue

Metabolic breakdown of	gives rise to
500 g fatty tissue	535 ml water of oxidation
500 g nonfatty tissue	75 ml water of oxidation + 365 ml intracellular water
1000 g fatty and nonfatty tissue together	610 ml water of oxidation + 365 ml intracellular water
Total: 975 ml water	

The breakdown of 1 kg of the body's own tissue, assuming made up of equal parts of fatty and nonfatty tissue, thus gives rise to about 1 l of endogenous, practically sodium-free water. It is important that this should be allowed for in patients with a high calorie consumption whose water excretion is low (e.g., after operations), since otherwise they may easily become waterlogged. A patient given only electrolytes and 5% glucose solution after uncomplicated abdominal operation should therefore lose 200 g weight per day¹⁰.

Water and Electrolyte Balance

(For references see page 530)

Electrolyte balance

Table 11 Daily requirements, usual intake and average excretion of various electrolytes^{1, 7, 10, 11}

	Minimum requirement*	Usual intake	Average excretion**			
			With an intake of mEq/day	Urine mEq/day	Faeces mEq/day	Sweat mEq/day
Sodium						
Adults.....	20	50-250	100	97	3	0-
Per square metre body surface.....	12	29-145				
Per kilogramme body weight.....	0.3	0.7-3.6				
Potassium						
Adults.....	20-33	50-150	100	90	10	0-
Per square metre body surface.....	12-19	29-87				
Per kilogramme body weight.....	0.3-0.5	0.7-2.1				
Calcium						
Adults.....	15	25-75	50	5	45	
Per square metre body surface.....	9	14-43				
Per kilogramme body weight.....	0.2	0.4-1.1				
Magnesium						
Adults.....	16-25	20-50	30	10	20	
Per square metre body surface.....	9-14	12-29				
Per kilogramme body weight.....	0.2-0.4	0.3-0.7				
Chloride						
Adults.....	20	50-250	100	97	3	0-
Per square metre body surface.....	12	29-145				
Per kilogramme body weight.....	0.3	0.7-3.6				

* For details see under 'Urine', pages 662-664, 'Faeces', page 65 'Sweat', pages 679-680

Table 12 Amounts and electrolyte contents of important body fluids*

	Amount	Sodium mEq/l	Potassium mEq/l	Chloride mEq/l	Bicarbonate mEq/l	pH
Saliva	500-1500 ml/24 h	10-25	15-40	10-40	2-13	-
Gastric juice	2000-3000 ml/24 h	-	-	-	-	-
with parietal-cell secretion	-	20-70	5-15	80-160	0	acid
without parietal-cell secretion	-	70-150	5-15	80-120	25-40	neutral to weakly alkaline
Pancreatic juice	300-1500 ml/24 h	140	6-9	110-130	25-45	alkaline
Bile	250-1100 ml/24 h	130-165	3-12	90-120	30	weakly alkaline
Intestinal secretions	3000 ml/24 h	-	-	-	-	weakly alkaline
Small intestine, Miller-Abbott tube	-	82-148	2-8	43-137	-	-
Ileostomy, stents	-	105-144	6-29	90-136	-	-
Ileostomy, adapted	-	46	3	21	-	-
Colectomy	-	53	8	-	-	-
Ileal-luminal fluid	500 ml	70	35	-	-	-
Sweat	500-1000 ml/24 h	5-80	5-15	5-70	-	-
Cerebrospinal fluid	100-160 ml	130-150	2.5-4.5	122-128	25	weakly alkaline
Transudates**	-	150-145	2.5-5	90-110	-	-
Faecal water***	-	-	-	-	-	-

* These data are discussed more fully in the later chapters dealing with the individual body fluids. The values for the intestinal secretions and transudates are from LOCKWOOD and RANDALL¹², those for the intraluminal fluid from BLANK¹³.

** The range of the electrolyte concentrations in transudate water is those in serum water amounts on the average to 0.9% for sodium, 0.92% for potassium.

Table 13 Sodium and potassium exchange in a man weighing 70 kg^{10,16}

	Sodium	Potassium
Total exchangeable*	2800 mEq	3400 mEq
In plasma.....	450 mEq	14 mEq
In interstitial fluid ..	1900 mEq	60 mEq
In intracellular fluid ..	220 mEq	3300 mEq
Average intake	100 mEq/24 h**	100 mEq/24 h***
Average excretion ..	100 mEq/24 h	100 mEq/24 h
1 mEq corresponds to	23 mg	39 mg

* Including sodium in the bones, which is not otherwise included in the table. For further details see 'Composition of the Body', page 518.

** 1 l of physiological (isotonic) salt solution (0.85%) contains 145 mEq each of sodium and chloride, which is more than the daily requirement of salt.

*** 60 mEq/day is adequate if given parenterally and kidney function is unimpaired¹⁰. Patients with healthy kidneys can safely be given infusions of 20–25 mEq potassium per hour; in severe potassium deficiency it may be necessary to give 50–60 mEq per hour¹⁶.

Osmotic relationships

The distribution of water and its solutes in the water spaces of the body is a result of the osmotic relationships. The membranes separating the various fluid phases of the body (the vascular endothelium and the cell membranes) are in general freely permeable to water, so that there is a uniform osmotic pressure throughout the body fluids. For a discussion of freezing-point depression, osmotic pressure, osmolality and osmolality see pages 270–271. For conversion tables see pages 272–273.

Freezing-point depression of plasma at 38°C: 0.540°C

Osmotic pressure of plasma at 38°C: 7.39 atm (5616 mm Hg)

Osmolality of plasma at 38°C: 291.2 mosm/kg water

The theoretical osmolality of blood plasma calculated from its known components and assuming their complete electrolytic dissociation is 325 mosm/kg serum water. The difference between this value and the actual osmolality of 291.2 mosm/kg serum water (the numerical value is about twice that of the sodium concentration in serum in mEq/l) is due to the fact that the electrolytes are not completely dissociated in serum.

Tonicity. From the clinical standpoint, tonicity and osmolality are the same thing. A solution is described as *isotonic* when it is osmotic with serum, i.e., has the same osmotic pressure as serum. In practice, both hypotonic and hypertonic solutions with osmolality ranging from 140 to 1710 mosm/kg water can be administered continuously without causing haemolysis¹. 1/6 molar, or 1/6 normal, solutions of all salts having binary dissociation can be regarded for practical purposes as isotonic (333 mosm/l).

The maintenance of the plasma volume and the distribution of fluid between the plasma and the interstitial space is mainly dependent on the 'effective' osmotic pressure of the plasma proteins. The capillary endothelium is freely permeable to almost all the substances in solution in the extracellular fluid, the total osmotic pressure of which is determined mainly by the sodium and chloride ions. However, since these ions pass freely through the capillaries and become uniformly distributed by diffusion and filtration throughout the extracellular space they cannot contribute to the osmotic pressure gradients between the intravascular and extravascular spaces. On the other hand, the intravascular space contains almost all the large protein molecules. As a result of their effective osmotic pressure, these molecules prevent the passage of water out of the plasma in spite of the fact that they are responsible for only a small part of the total osmolality. This specific effect of the plasma proteins is known as the *colloid-osmotic* or *oncotic pressure*.

Oncotic pressure of plasma at 38°C: ca. 0.04 atm
ca. 30 mm Hg
ca. 400 mm H₂O

The albumins contribute about 85% of the colloid-osmotic pressure. Since fibrinogen has practically no osmotic effect its high molecular weight the colloid-osmotic pressure can be assumed to be the same as that of plasma.

When the composition of the plasma proteins is known the colloid-osmotic pressure can be calculated by means of the formula of KEYS¹⁷:

$$\text{Colloid-osmotic pressure (in mm H}_2\text{O)} = f_c (4.52 A + 1.886 G) \times 10^3$$

where A = albumin concentration in g/l, G = globulin concentration in g/l, T = absolute temperature in kelvin (K) = 273 + t , f_c = a factor whose value depends on the total protein concentration in the serum as follows:

Total protein content of serum (g/l)	10	20	30	40	50	60
f_c	0.88	0.92	0.98	1.03	1.09	1.17

The colloid-osmotic pressure is counteracted by the hydrostatic pressure in the capillaries.

Capillary pressure at 38°C (see also page 553):

Arterial limb	32 mm Hg 435 mm H ₂ O
Venous limb	12 mm Hg 163 mm H ₂ O

For osmotic activity of serum electrolytes see Table 3, page 530.

Table 14 Osmotic activity of serum crystalloids¹⁰

1000 mg glucose/l serum	5.5 n
1000 mg urea/l serum	17.2 n

Table 15 Osmotic activity of serum colloids¹⁰

	g/l	mEq/l
Albumin	45	14
Globulin	15	2
Total proteins	60	16

Infusions of plasma and blood are distributed throughout the intravascular space, those of isotonic electrolytes throughout the extracellular space, those of isotonic crystalloid solutions (glucose solutions) throughout the total body water.

Caloric requirements

The definition of the caloric and conversion tables will be found on pages 212–213, the daily caloric requirements on page 530, caloric values of foods on pages 498–515, and the caloric values of fats, proteins and carbohydrates on page 539.

The caloric requirements in parenteral infusion therapy met by solutions of carbohydrates and amino acids and by emulsions of fats. Commercial preparations of known caloric value are available.

The human body cannot normally utilize more than ca. 0.5 g glucose per kilogram body weight per hour¹⁸.

Ethyl alcohol 95 vol% furnishes 5.6 kcal/g, lactate 0.31 kcal/g. 250 ml of plasma contain 15 g protein, equivalent to ca. 60 kcal.

The total caloric consumption and expenditure of a healthy patient who is not bedridden but whose activity is limited are about approx. 2000 kcal per day.

(For references see page 530)

Table 16 Daily calorie balance of a man weighing 70 kg^{1,2}

Average intake		Average excretion	
100 g fat + carbohydrate + protein		12 g urea nitrogen	
150 l oxygen		450 l carbon dioxide	
		300 ml water of oxidation	
	Energy in kcal		Energy in kcal
Fat	900	Bodily activity (light) ..	800
Carbohydrate ..	1400	Specific dynamic effect ..	200
Protein	300	Basal metabolism	1600
Total	2600	Total	2600

Acid-base balance and pH

The concentration of hydrogen ions in the various water compartments of the body is determined by the amounts and proportions of acids and bases present. It is maintained within definite limits

present, changes in the electrolyte content of the body fluids often cause changes in pH and vice versa

Table 17 Buffer capacity ($\Delta\text{mEq}/\Delta\text{pH}$) of the body tissues²⁰

Tissue	Buffer capacity per kilogramme tissue	Kilogramme tissue per kilogramme body weight	Buffer capacity per kilogramme body weight
Blood	18	0.10	1.8
Muscle	5	0.65	3.25

Table 18 Relative buffer capacity of blood²¹

Whole blood 100%	Cells	79%	Ionized protein 13.6% Bicarbonate 6.1% Phosphate 1.5%
	Plasma	21%	

On a normal mixed diet the body has a positive hydrogen-ion balance. The hydrogen ions arising from the breakdown of foods

$$\text{pH} = 6.10 + \log \frac{[\text{total CO}_2]_p - 0.0301 P_{\text{CO}_2}}{0.0301 P_{\text{CO}_2}}$$

where $[\text{total CO}_2]_p$ = sum of the concentrations of dissolved CO_2 and HCO_3^- in the plasma (p = plasma) in mmol/l. Conversion into vol% is made as follows (see page 276):

$$\text{mmol/l} = \frac{\text{vol}\%}{2.226}$$

The sum of the concentrations of dissolved CO_2 and H_2CO_3 in the plasma (in mmol/l) can be calculated from the formula:

$$[\text{CO}_2]_p = 0.0301 P_{\text{CO}_2}$$

The concentration of HCO_3^- in the plasma (in mmol/l) is obtained as the difference between the total CO_2 concentration and the concentrations of dissolved CO_2 and H_2CO_3 :

$$[\text{HCO}_3^-]_p = [\text{total CO}_2]_p - [\text{CO}_2]_p$$

These relationships are shown diagrammatically in Figure 1 (page 528).

Table 19 Normal values for the CO_2 -bicarbonate system in the arterial and venous blood of adults^{22, 23}

	Unit	Blood sample ²²	Mean	Range
pH	—	p	7.37	7.32-7.42
$[\text{HCO}_3^-]_p$	mmol/l	p	26	24-28
P_{CO_2}	mm Hg	p	40	34-46
$[\text{total CO}_2]_p$	mmol/l	p	27	25-29
$[\text{CO}_2]_p$	mmol/l	p	25	23-27
		v	1.38	1.26-1.65
		v	1.20	1.02-1.38

* For persons living at sea level.

²² p = arterial blood, v = venous blood.

The respiratory components of the acid-base balance are adequately expressed by the P_{CO_2} value, whereas the metabolic components are best expressed by the plasma bicarbonate content²², by the base excess content of the whole blood²³ (see page 571), or by the base excess of the whole blood²⁰ (see page 571) is a matter of discussion²⁴.

The following changes in acid-base balance are distinguished on the basis of the origin of the disturbance:

1. Respiratory alkalosis. Decrease in P_{CO_2} as a result of hyperventilation.
2. Respiratory acidosis. Increase in P_{CO_2} as a result of reduced CO_2 excretion by the lungs.

¹ According to the Bland-White-Lowry definition, acids are proton donors (hydrogen donors), bases proton acceptors.

3. Metabolic alkalosis: Increase in the base content or decrease in the acid content of the blood.
4. Metabolic acidosis: Increase in the acid content or decrease in the base content of the blood.

Two of these disturbances may appear at the same time (cf. Fig. 2).

Fig. 1 Nomogram for the evaluation of the HENDERSON-HASSELBALCH formula²⁶

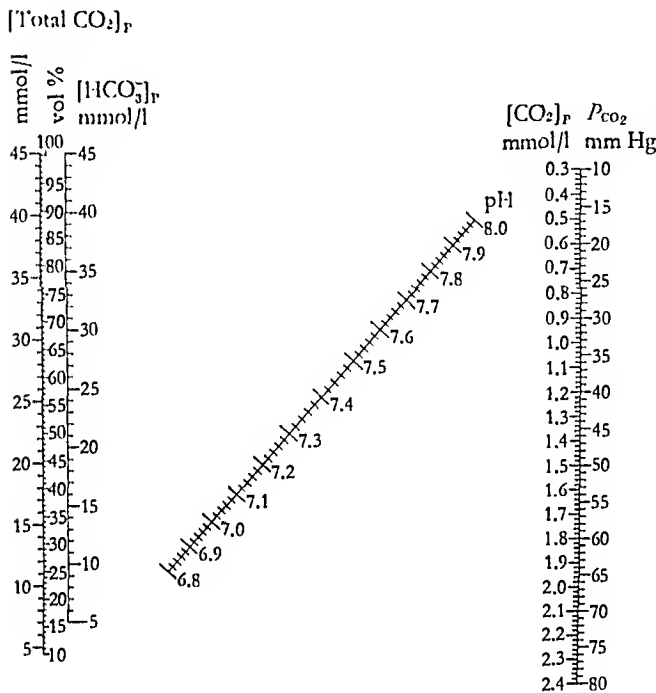
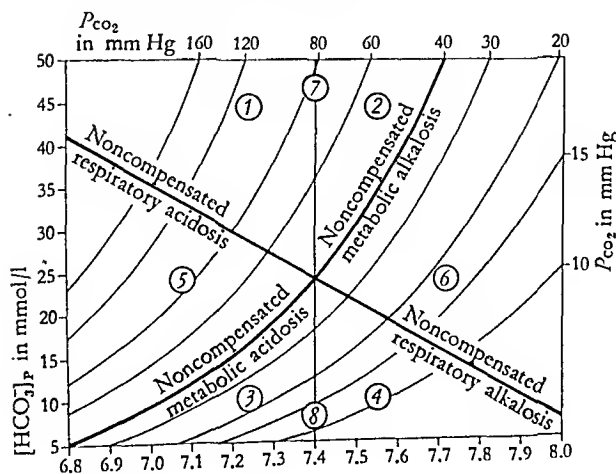


Fig. 2 The pH-bicarbonate diagram of DAVENPORT²⁵ as modified by PERRET³²

The heavy line running from upper left to lower right is the normal plasma buffer curve, that running from lower left to upper right the P_{CO_2} isobar for normal plasma (40 mm Hg); other P_{CO_2} isobars are shown by thinner lines. The point of intersection of the plasma buffer curve and the 40 mm Hg isobar represents blood with the normal values pH = 7.40, bicarbonate concentration = 24 mmol/l, P_{CO_2} = 40 mm Hg.

The numbers in the diagram denote areas in which there is disturbance of acid-base balance: 1 Compensated respiratory acidosis, 2 Compensated metabolic alkalosis, 3 Compensated metabolic acidosis, 4 Compensated respiratory alkalosis, 5 Respiratory and metabolic acidosis, 6 Metabolic and respiratory alkalosis, 7 Fully compensated respiratory acidosis or metabolic alkalosis, 8 Fully compensated metabolic acidosis or respiratory alkalosis.



Blood volume

Table 20 Blood volume in health^{*10}

Body build	Blood volume as per cent of body weight	
	Men	Women
Normal	7.0	6.5
Obese	6.0	5.5
Thin	6.5	6.0
Muscular	7.5	7.0

* Based on measurements of absolute blood volume made by separate simultaneous determination of plasma volume and red cell volume using two different tracer substances and addition of the results. For a detailed discussion of blood volume see pages 554-555.

Body surface area

Table 21 Surface area of various parts of the body as percent of total body surface³³

Age in years	Head	Trunk*	Arms**	Legs
0	19	34	19	28
1	17	34	19	30
5	13	34	19	34
10	11	34	19	36
15	9	34	19	38
Adults	7	34	19	40

* Including the neck, genitals and buttocks.

** At all ages the palm of the hand is about 1% of the total body surface

Table 22 Rule of nines for adults^{*34}: Surface area of various parts of the body as percentage of total body surface

Head	9
Arms, each	9
Trunk, front	18
Trunk, back	18
Legs, each	18
Genitals	1
Total	100

* The buttocks are included in the lower limbs. The proportions are sufficiently accurate for clinical purposes.

Parenteral therapy

Patients should be fed by mouth as soon as this is feasible. When intravenous water and electrolyte infusions are necessary at least part of the patient's nourishment should be by mouth if possible.

Infusions should not be given subcutaneously; absorption is slow and irregular (diffusion of ions and water), the procedure is painful, the amount of fluid that can be given is limited, and the risk of infection is greater than when the intravenous route is used. more than one infusion must be given, early installation of intravenous tube is advisable. In the event that the tube must be left in situ for several days it is best to use the cephalic, basilic or jugular vein and introduce it as far as the superior vena cava. This method appears to involve less risk of thrombosis than the use of the saphenous vein and the inferior vena cava. The smaller veins of the arms or legs can be used, however, if the infusion is of short duration and the solutions are more or less isotonic.

I. Nomogram for number of drops per minute³⁹

The number of drops per minute required to administer a particular quantity of infusion solution in a certain time can be read off directly from this nomogram. The nomogram allows for the increase in drop size as the dropping rate increases and is based on the normal drop defined by the relationship: 20 drops distilled water at 15°C = 1 g (± 0.05 g) when falling at the rate of 60/min. The dependence of drop size on dropping rate is allowed for by the increasing width of the scale units of the three abscissae as the dropping rate increases.

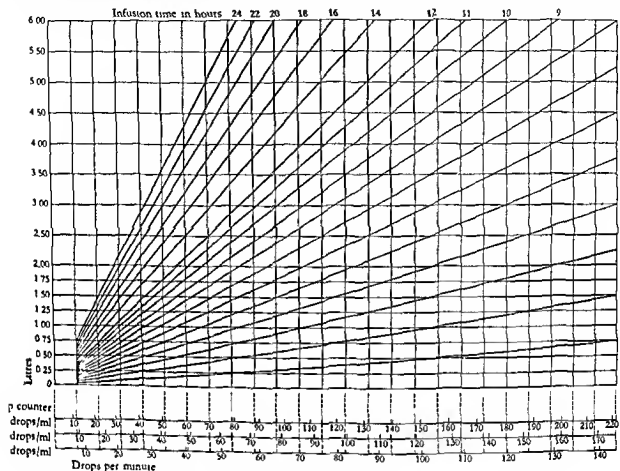


Table 23 Composition of some important parenteral infusion solutions

Solution	Solute	g/l	Na ⁺ mEq/l	K ⁺ mEq/l	Ca ⁺⁺ mEq/l	Mg ⁺⁺ mEq/l	Cl ⁻ mEq/l	HCO ₃ ⁻ mEq/l	Lactate mEq/l	Total ions mEq/l	moam/l	kcal/l
Glucose 5%	C ₆ H ₁₂ O ₆	50	-	-	-	-	-	-	-	-	278	200
Salt 0.85%	NaCl	8.5	145	-	-	-	145	-	-	290	290	-
RINGE (USP)	NaCl	8.6	147	-	-	-	147	-	-	-	-	-
	KCl	0.3	-	4	-	-	4	-	-	-	-	-
	CaCl ₂ + 2H ₂ O	0.33	-	-	5	-	5	-	-	-	-	-
	Total	-	147	4	5	-	156	-	-	312	309	-
RINGER lactate (HARTMANN)	NaCl	6.0	103	-	-	-	103	-	-	-	-	-
	KCl	0.4	-	5.4	-	-	-	-	-	-	-	-
	CaCl ₂ + 6H ₂ O	0.2	-	-	1.8	-	5.4	-	-	-	-	-
	Na lactate	3.05	27	-	-	-	1.8	-	-	-	-	9
	MgCl ₂	0.2	-	-	-	2	-	-	27	-	-	-
	Total	-	130	5.4	1.8	2	112.2	-	27	278.4	276	9
Sodium bicarbonate 1/4 normal	NaHCO ₃	14	167	-	-	-	-	167	-	334	334	-
Ammonium chloride 1/4 normal	NH ₄ Cl	9	-	-	-	-	169	-	-	338	338	-

Table 24 Order of priority in the parenteral therapy of acute disturbances of water and electrolyte balance¹⁰

1. Maintenance of blood volume	5. Administration of potassium (see Table 13)
2. Maintenance of colloid-osmotic pressure	6. Total body water and electrolytes: maintenance of requirements and elimination of deficits
3. Restoration of acid-base balance	7. Provision of calories
4. Restoration of total osmotic pressure	

A great variety of crystalloid and electrolyte solutions of known constitution are commercially available. The tendency is now to restrict parenteral infusion therapy to a minimum number of basic solutions meeting the daily water and electrolyte requirements. Ampoules containing other electrolytes are available for mixing with these solutions if the need arises. Potassium chloride and lactate, sodium chloride, bicarbonate and lactate, calcium chloride, magnesium sulphate and others are supplied in this form.

Metabolic disturbances of acid-base balance mostly require treatment with sodium bicarbonate, sodium lactate, ammonium chloride or arginine hydrochloride. An effective intracellular buffer is also now available in the form of tris-hydroxymethylamino-methane (THAM). Its 0.3-molar solution (36.3 g/l) is isotonic and is usually given at a dosage of 0.3–0.5 g/kg body weight over 3–4 hours²⁶.

The following colloidal solutions are in common use in parenteral infusion therapy:

1. Whole blood: available as stored citrated blood, fresh citrated blood, fresh blood drawn over cation exchangers, fresh heparinated blood, or blood given by direct transfusion.
2. Red-cell concentrates: in their own plasma or in isotonic electrolyte solutions.
3. Plasma and plasma fractions: available as dried human plasma (not free of hepatitis virus), pasteurized plasma protein solutions, fresh plasma, or solutions of albumin, fibrinogen, antihæmophilic globulin and gamma globulin.
4. Plasma expanders in the form of dextran solutions (average molecular weight of either 70 000 or 40 000).

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(For references see page 536)

The individual functions of the kidneys can be assessed by means of quantitative as well as so-called semiquantitative tests. The quantitative tests are mostly based on the clearance principle and their use is not in all cases practicable or necessary; some are very time-consuming and may involve referring the patient to a specialized clinic. The semiquantitative tests include determinations of nonprotein nitrogen (NPN) and 'true' endogenous creatinine in the plasma, the phenolsulphonphthalein (PSP) test, and the fluid deprivation test for determining the ability of the kidneys to concentrate urine. The sensitivity of semiquantitative tests can be established by comparing their results with those of precise quantitative methods of determining the renal functions concerned.

Renal haemodynamics

Quantitative methods

In these tests the plasma clearance (C)^{1,2} of certain substances is calculated by means of the formula:

$$C = \frac{U \times V}{P} \quad (1)$$

where U and P are the concentrations of the clearance substance in

the urine and plasma respectively.

For the determination of the renal plasma flow (RPF) the substance used is ⁵¹Cr-EDTA.

For the determination of the effective renal plasma flow (ERPF) the substance used is ¹²⁵I-iothalamate.

For the determination of the glomerular filtration rate (GFR) the substance used is inulin or creatinine.

For the determination of the renal blood flow (RBF) the substance used is ¹³³Xe.

It has recently been shown³ that a poly(fructose)saccharide resembling

inulin is superior to all other substances for the determination of the effective renal plasma flow (ERPF).⁴

On account of its physicochemical and physiological properties, ⁵¹Cr-EDTA and (PAH) is superior to all other substances for the determination of the effective renal plasma flow (ERPF).⁵

$$C_{PAH} = \frac{U_{PAH} \times V}{P_{PAH}} \quad (2)$$

The total renal plasma flow^{2,12}

$$RPF = \frac{C_{PAH}}{f_{PAH}} \quad (3)$$

$$E_{PAH} \text{ is the renal extraction } E_{PAH} = \frac{K_2 - K_1}{K_2}$$

where K_2 is the concentration of PAH in the renal vein and K_1 is the concentration of PAH in the renal artery.

The effective renal blood flow^{2,12}

$$\text{The effective renal blood flow}^2 = \frac{C_{PAH}}{1 - Ht} \quad (4)$$

(Ht = peripheral haematocrit value)

The total renal blood flow^{2,12}

$$RBF = \frac{C_{PAH}}{E_{PAH} (1 - Ht)} \quad (5)$$

The 'normal' value of the renal plasma flow is 1.2 l/min.

The 'normal' value of the renal blood flow is 1.2 l/min.

The 'normal' value of the effective renal plasma flow is 1.2 l/min.

The 'normal' value of the effective renal blood flow is 1.2 l/min.

The 'normal' value of the glomerular filtration rate is 120 ml/min.

The 'normal' value of the renal blood flow is 1.2 l/min.

The 'normal' value of the effective renal plasma flow is 1.2 l/min.

The 'normal' value of the effective renal blood flow is 1.2 l/min.

The 'normal' value of the glomerular filtration rate is 120 ml/min.

The 'normal' value of the renal blood flow is 1.2 l/min.

The 'normal' value of the effective renal plasma flow is 1.2 l/min.

The 'normal' value of the effective renal blood flow is 1.2 l/min.

The 'normal' value of the glomerular filtration rate is 120 ml/min.

The 'normal' value of the renal blood flow is 1.2 l/min.

The 'normal' value of the effective renal plasma flow is 1.2 l/min.

The 'normal' value of the effective renal blood flow is 1.2 l/min.

portion, so that the filtration fraction remains practically unchanged. The standard values at any age are given by the following equations:

$$C_{Cr} = 157.0 - (1.16 \times \text{age in years})$$

$$C_{PAH} = 820.2 - (6.75 \times \text{age in years})$$

The renal fraction of the minute output of the heart amounts normally to about 20%².

Semiquantitative methods

There exists no simple linear relationship between the glomerular

filtration rate and the plasma creatinine concentration.

The relationship between the glomerular filtration rate and the plasma creatinine concentration is

hyperbolic, so that the glomerular filtration rate decreases

as the plasma creatinine concentration increases.

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as the plasma creatinine concentration increases.

Table 1 Normal values in renal haemodynamics (based on a body surface area of 1.73 m²)

1 Normal conditions (mixed diet, urinary volume 1-3 ml/min)		
Women ²	C_{Cr}	108.8 ± 13.3 ml/min
	C_{PAH}	592 ± 153 ml/min
	FF	0.194 ± 0.039
	RBF ²	982 ± 184 ml/min
Men ²	C_{Cr}	124.1 ± 25.8 ml/min
	C_{PAH}	654 ± 163 ml/min
	FF	0.192 ± 0.035
	RBF ²	1209 ± 256 ml/min
Men and women ¹³	C_{Cr}	124.5 ± 9.7 ml/min
	C_{PAH}	638.6 ± 84.5 ml/min
	FF	0.197 ± 0.018
	RBF ¹²	1165 ml/min
2 Hydration (urinary volume 6-12 ml/min)		
Men and women ¹⁴	C_{Cr}	152.6 ± 14.7 ml/min
	C_{PAH}	711.7 ± 136.5 ml/min
	FF	0.220 ± 0.037
3 Steady state in dietetic restriction of sodium to 30 mEq/day, protein intake 0.5-1.0 g/kg body weight/day, urinary volume 1-3 ml/min		
Men and women ¹⁵	C_{Cr}	107.6 ± 11.4 ml/min
	C_{PAH}	631.2 ± 87.8 ml/min
	FF	0.172 ± 0.018

* This chapter on 'Renal Function Values' has been compiled by D. P. MEYER and H. SARRS, Medical Policlinic, University of Freiburg i. B. (Director: Prof. H. SARRS).

The upper limit of the normal range of plasma NPN concentration considered to be 40 mg/100 ml²⁴. Increases in this level are known to be dependent on an increase in the urea fraction. The proportion of the NPN due to the urea nitrogen can be calculated roughly from the urea nitrogen by means of the formula of PETERS and VAN SLYKE²⁵:

$$\text{NPN (in mg/100 ml)} = 10 + (1.07 \times \text{urea-N in mg/100 ml}).$$

Here it should be borne in mind that in chronic renal insufficiency the rise in the NPN is not due to urea nitrogen to the extent indi-

cated by the above formula. Whereas in acute renal failure up to 90% of the NPN is represented by urea, in chronic renal insufficiency there is a relatively larger increase in other NPN components.

The 15-minute *phenolsulphonphthalein* test (after a single i.v. injection of 6 mg of the dye) is not sufficiently sensitive to reveal small changes in the excretory function of the renal tubules²⁶. The marked variance of the sample values around the regression line (Fig. 3) is due in the main to the combination of PSP with plasma proteins (dependent on various factors), the absence of a flo-

Fig. 1 Nonlinear relationship between the concentration of 'true' endogenous creatinine in plasma (P_{Cr} , as measured by the method of LOKEN²⁷) and the renal inulin clearance (C_{In}). $T_y = 95\%$ tolerance range for Y/x^{18}

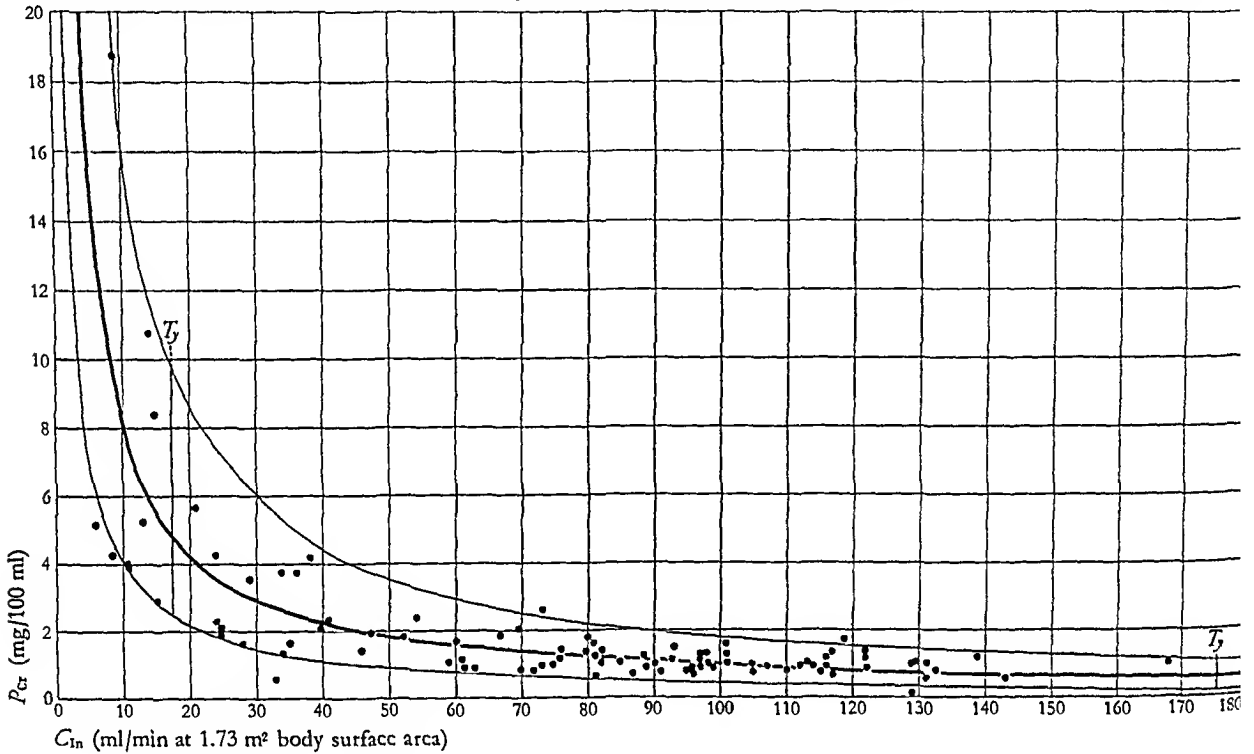
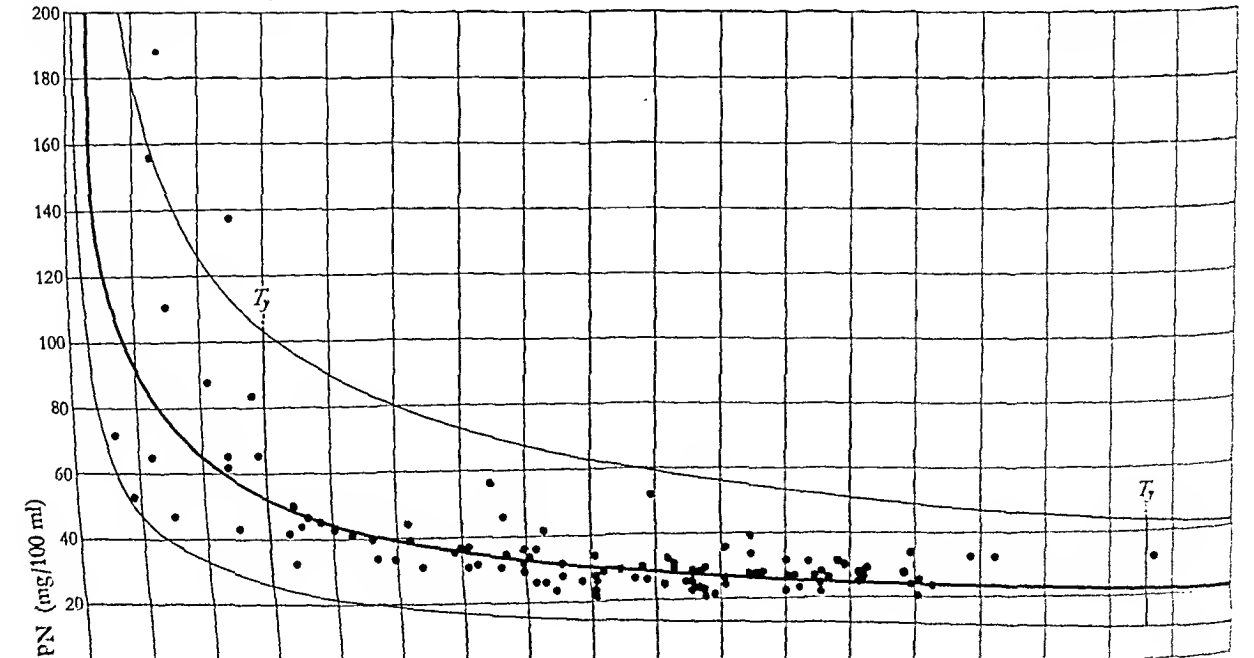


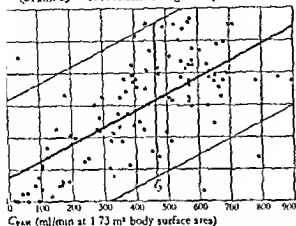
Fig. 2 Nonlinear relationship between the concentration of nonprotein nitrogen (NPN) in plasma and the renal inulin clearance (C_{In})¹⁹



Renal Function Values

(For references see page 536)

Linear relationship between the percentage excretion of phenolsulphonphthalein (PSP, 15-minute value after a single i.v. injection of 6 mg) and the renal PAH clearance (C_{PAH}). $T_y = 95\%$ tolerance range for Y/x^{24}



librium of PSP in the body fluid compartments after a single cation, failure to take account of body weight in evaluating the $\Delta t_{1/2}$, and the use of spontaneous urine samples²⁴

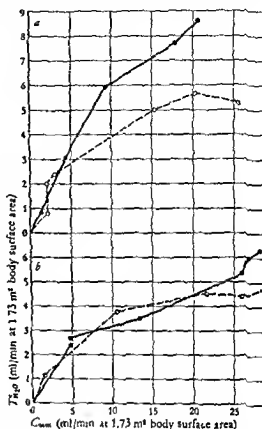
ution and concentration of urine

limits of the diluting capacity of the kidneys are usually now perished with. If the organ can concentrate urine it must also be

antidiuretic methods

When ADH (antidiuretic hormone) activity is at a maximum, the urinary concentrating capacity is limited by two factors²⁵ (a) during hydropenia and oliguria by the maximum value of the ratio between the osmotic concentrations of the urine and plasma

Fig 4 Plots of T_{H_2O} during saline diuresis (—) or diuresis (---) in (a) a healthy man and (b) essential hypertension²²



a tendency to decrease (Fig 4). In contrast to the vie

Normal values

Maximum urinary osmolarity	900–1400 mosm/l ²²⁻²³ 1027 ± 110 mosm/l ²² 1067 (918–1230) mosm/l ²²
Maximum value of U_{osm}/P_{osm}	2.77 ± 0.36 ²² 3.63–4.65 ²³
T_{H_2O} (with i.v. infusion of hypertonic mannitol solution)	57 ± 20 ml/min ²²
$T_{H_2O} \times 100/C_{H_2O}$ (with i.v. infusion of hypertonic mannitol solution)	51 ± 15 ²²

At maximum diuresis the excess of osmotically free compared to a hypothetical osmotic urinary portion can be as the maximum free-water clearance (T_{H_2O}).

Normal values (1.73 m² body surface area)

$T_{H_2O}^{\text{max}}$ = maximum C_{H_2O}	17.1
	23.1

(For references see page 536)

Fig. 5 Diagram for reading off values of Tm_{H_2O} from those of U_{osm}/P_{osm} and the simultaneous urinary minute volume in osmotic diuresis⁴³

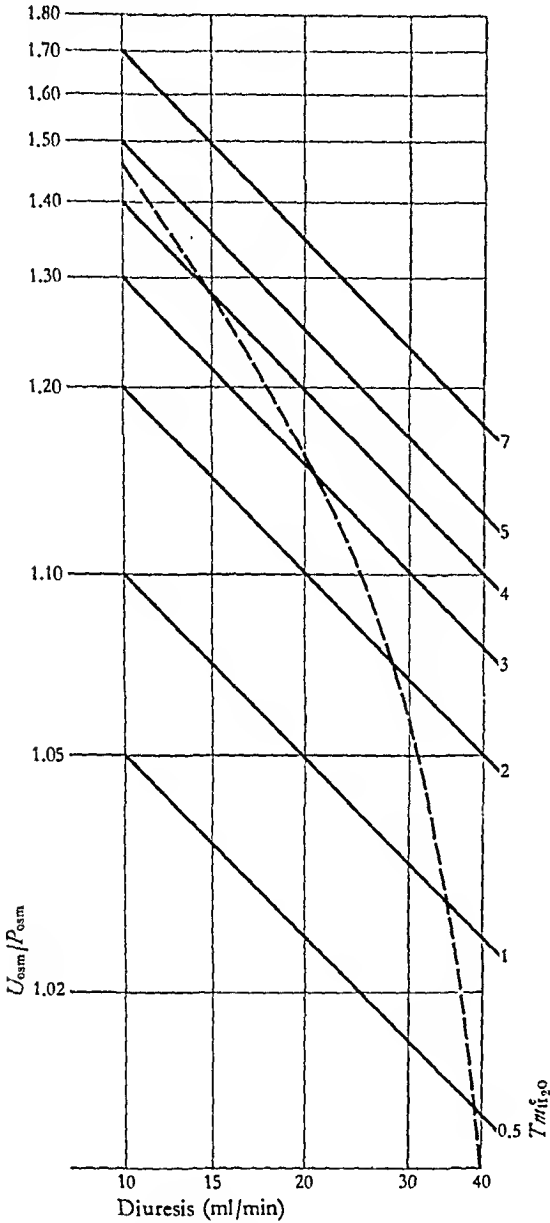
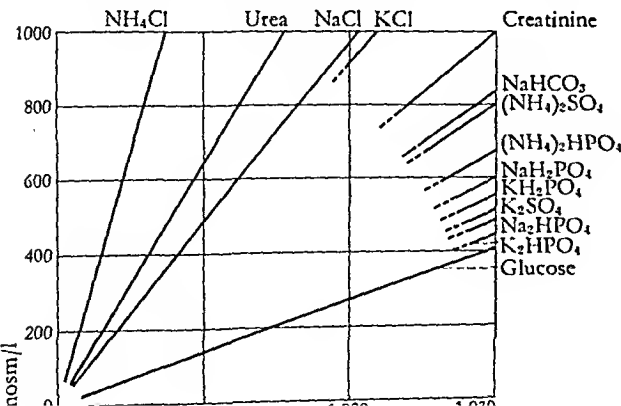


Fig. 6 Contributions of various urinary components to the specific gravity and osmolarity of the urine⁴⁹



There are considerable discrepancies in the 'normal' values given in the literature for some of the parameters of renal concentrating capacity, a result of differences in the experimental methods. The concentrating capacity of the kidneys can be increased by means of a protein-rich diet⁴⁴; it is decreased under conditions of inadequate dehydration⁴⁵ and in man (fluid deprivation test) is independent of the sodium chloride intake⁴⁶.

For persons between the ages of 24 and 72 years with healthy kidneys the age dependence of maximum urinary osmolality as found by a 24-hour fluid deprivation test is given by the formula⁴⁷:

$$U_{osm} \text{ (in mosm/l)} = 1134 - (4.1 \times \text{age in years})$$

Semiquantitative methods

While the underlying physiological process in the concentration of urine consists of the removal of osmotically-free water, the various electrolytes and nonelectrolytes present contribute in different degrees to the specific gravity and osmotic pressure. The determination of the maximum specific gravity of urine in the fluid deprivation test⁴⁸ must therefore be regarded as a semiquantitative test of renal function.

Glucose, phosphate and sulphate cause a high specific gravity of urine at fairly low osmotic concentrations⁴⁹, whereas chloride and urea exert a relatively high osmotic pressure for a given urinary specific gravity (Fig. 6). In persons with healthy kidneys the maximum urinary osmolality reached in the fluid deprivation test is only loosely related to the maximum specific gravity²⁹. The variance in the relationship between these two parameters increases in renal disease (Fig. 7)³⁰.

Normal specific gravity of urine (24-hour fluid deprivation test)	1.035 \pm 4 ²⁷
Lower limit of the normal (healthy kidney)	1.026 ^{24, 27, 30}

The maximum urinary specific gravity falls from an average of 1.032 at 20 years to an average of 1.024 between 80 and 90 years⁵⁰.

Dependence of the 24-hour urinary volume on the amounts of solutes removed in the urine and the concentrating capacity of the kidneys

The amounts of solutes removed in the urine depend both on the dietary intake, particularly of proteins and salts, and on the caloric turnover of the body⁵¹. A mixed diet yields about 1200 mosm of urinary solutes per day⁵², an amount reduced by fasting to about 800 mosm. In fasting subjects given 100 g glucose per day the urinary solutes fall to 400 mosm per day, while a diet low in protein and salt but rich in carbohydrates (with maintenance of the basal metabolic rate) results in a further reduction to 200 mosm per day. On the basis of a maximum urinary osmolality of 1400 mosm/l the amounts of water required for the excretion of these amounts are 857, 571, 286 and 143 ml respectively. In isosthenuria (urinary osmolality of 300 mosm/l) the renal elimination of 1200, 800, 400 and 200 mosm of urinary solutes requires respectively 4000, 2667, 1333 and 667 ml of water. The relationship between the renal water requirement and the urinary osmolality for different daily amounts of solutes removed in the urine is shown in Figure 8⁵¹.

Tubular transport functions

Clearance techniques enable an assessment to be made of the state of functioning of the active local transport mechanisms in the proximal tubular convolution. Both the tubular secretion of *p*-aminohippuric acid (PAH) and the reabsorption of glucose (G) from the tubular urine are limited by transport maxima (Tm)¹.

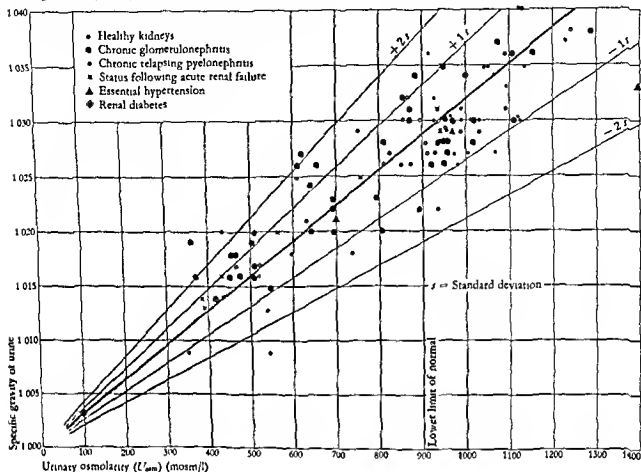
$$Tm_{PAH} = (U_{PAH} \times V) - (P_{PAH} \times C_{in} \times k)^9 \quad (11)$$

where U_{PAH} and P_{PAH} are the concentrations of PAH in urine and plasma respectively and k is a correction factor for the plasma PAH fraction that is protein-bound and not filtrable by the glomeruli. The normal value of k is 0.83.

$$Tm_G = (P_G \times C_{in}) - (U_G \times V) \quad (12)$$

Normal values (for 1.73 m ² body surface area)	
Tm_{PAH} Men	79.8 \pm 16.7 mg/min ²
Women	77.2 \pm 10.8 mg/min ²
Tm_G Men	375 \pm 79.7 mg/min ^{1.2}
Women	303 \pm 55.3 mg/min ^{1.2}

Fig 7 Relationship between the maximum urinary specific gravity (SU) achieved in the 18-hour fluid deprivation test and the corresponding osmolality (U_{osm}) of the urine: $(SU - 1.000) \times 1000/U_{\text{osm}} = 0.0318 \pm 0.0053^{20}$



These renal functions can be differentiated more precisely by relating T_{MPAH} (as a measure of the functioning secretory renal tissue) and T_{wo} (as a measure of the reabsorptive renal tissue) to C_{10} and C_{PAH} respectively. The ratios C_{10}/T_{MPAH} and T_{wo}/C_{10} are measures of glomerular activity, i.e., of the effective renal plasma flow per unit of the secretory or reabsorptive tissue.

Normal values

C_{10}/T_{MPAH}	$1.54 \pm 0.4 \text{ ml/mg}^2$
$C_{\text{PAH}}/T_{\text{MPAH}}$	$8.28 \pm 2.2 \text{ ml/mg}^2$
T_{wo}/C_{10}	$2.41 \pm 0.35 \text{ mg/ml}^2$

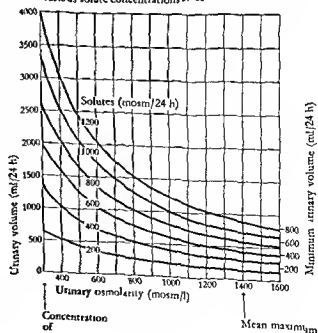
All these functions show age regression between the 20th and 90th years of life

$$\begin{aligned} T_{\text{MPAH}} &= 120.6 - (0.865 \times \text{age in years})^{24} \\ T_{\text{wo}} &= 432.8 - (2.604 \times \text{age in years})^{20} \\ C_{10}/T_{\text{MPAH}} &= 1.382 - (0.00158 \times \text{age in years})^{20} \\ C_{\text{PAH}}/T_{\text{MPAH}} &= 7.710 - (0.0278 \times \text{age in years})^{20} \end{aligned}$$

Excretion of acids and electrolytes

The total acid excretion (A_{H^+}) is made up of potentially ionizable hydrogen ions (titratable acidity, TA) and bound (nonionizable) hydrogen ions in the form of ammonium ions (NH_4^+).

Fig 8 Relationship between urinary volume and osmolality at various solute concentrations^{21, 22}



Normal values (on a mixed diet)

Total acid excretion (A_{H^+})	30–80 mEq/24 h ⁵³
Titrateable acidity (A_{TA})	10–30 mEq/24 h ⁵³
NH_4^+ excretion ($A_{NH_4^+}$)	20–50 mEq/24 h ⁵³
$A_{NH_4^+}/A_{TA}$	1.0–2.5 ⁵³
	1.28 ± 0.14 ⁶⁴

The difference between the sum of the TA and NH_4^+ excretions and the bicarbonate excretion (HCO_3^-) is known as the *effective acid excretion* ($A_{H^+_{eff}}$).

$$A_{H^+_{eff}} = A_{H^+} - A_{HCO_3^-} = A_{TA} + A_{NH_4^+} - A_{HCO_3^-} \quad (14)$$

In alkaline urine the effective acid excretion has a negative value since mainly bicarbonate ions are excreted.

The pH value of urine may vary between 4.6 and 8.2^{2, 55}.

An accurate assessment of the tubular treatment of an *electrolyte* from the excreted proportion of the amount filtered by the glomeruli is possible only when the substance concerned is freely filtrable and is exclusively reabsorbed in the tubules and not secreted. The only important electrolytes at present considered to fulfil this condition in man are sodium, chloride and bicarbonate.

Table 2 gives the mean values for the glomerular filtration and total excretion of some electrolytes in the 24-hour urine²⁴.

The *glomerular filtration rate* (GFR) of a completely filtrable electrolyte (E) is calculated as follows:

$$GFR_E \text{ (in mEq/min)} = k \times P_E \times C_{in} \quad (15)$$

where P_E is the plasma concentration of the electrolyte (in mEq/l) and k a correction factor for the small differences between the concentrations in plasma and glomerular filtrate resulting from the GIBBS-DONNAN equilibrium and the lowering of the water content of the plasma by the proteins.

The value of k is normally 1.02 for Cl^- and HCO_3^- ⁵⁶, 0.96⁶⁷ for Na^+ and 0.92⁶⁷ for K^+ .

For calculation of the amounts of partly plasma-protein-bound electrolytes filtered by the glomeruli it is important to know the

filtrable part. This is dependent on the concentration and composition of the plasma proteins and on the pH value and other physicochemical conditions. 54% of the plasma calcium and 68% of plasma magnesium are normally ultrafiltrable⁵⁸.

So-called 'normal' values for the clearance of electrolytes of little significance since they are very largely dependent on exogenous factors.

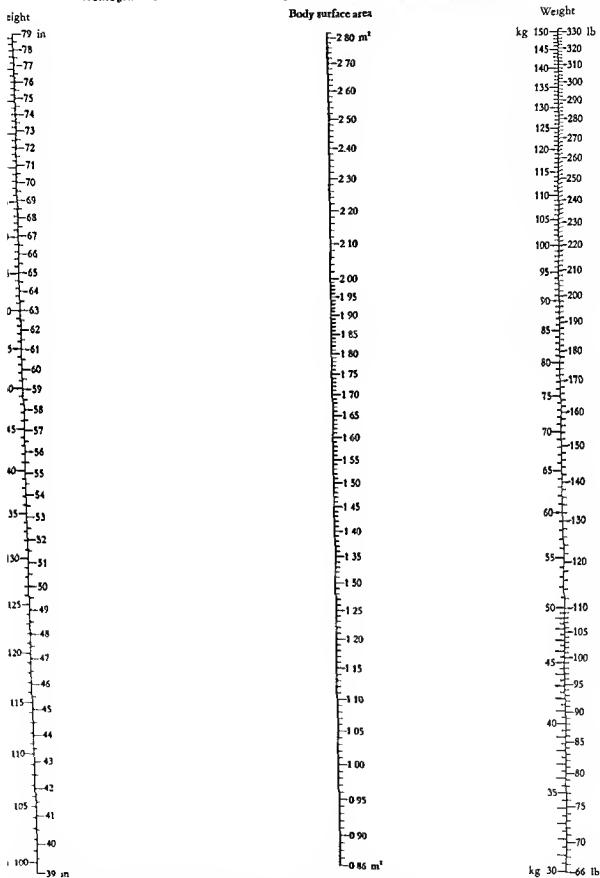
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Table 2 Amounts of solutes excreted and reabsorbed assuming a glomerular filtrate of 130 ml/min

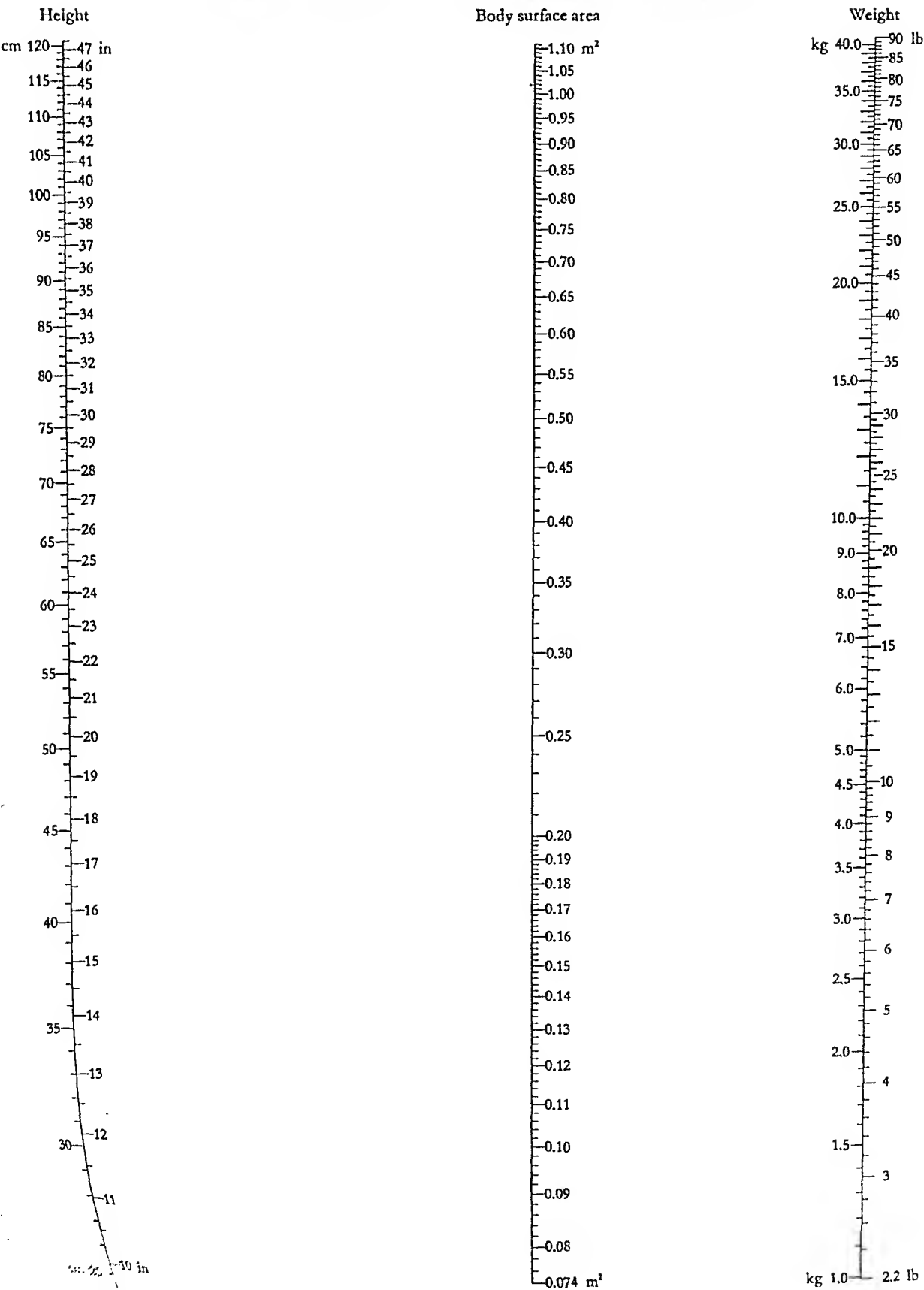
	Amount filtered	Amount excreted in urine
Urea	46 g	20–35 g
Uric acid	7.2 g	0.1–2 g
Amino acids	50 g	0.5–1 g
Creatinine	1.2 g	1.2–1.5 g
Glucose	180 g	–
Albumin	36 g	–
Sodium	600 g	4–6 g
Chloride	640 g	6–9 g
Potassium	7.2 g	2.5–3.5 g
Bicarbonate	4900 mEq	1–2 mEq
Calcium	uncertain	0.01–0.3 g
Inorganic phosphate (as P)	5.6 g	1–5 g
Inorganic sulphate (as S)	2.9 g	1.4–3.3 g
Water	180 l	1.5 l

Nomogram for determination of body surface area from height and weight



from the formulae of Du Bois and Du Bois, *Arch Intern Med*, 17, 863 (1916). $S = W^{0.725} \times H^{0.725} \times 71.84$, or $S = \log W \times 0.425 + \log H \times 0.725 + 1.8564$ (S = body surface in cm², W = weight in kg, H = height in cm)

Nomogram for determination of body surface area from height and weight



Formula of Du Bois and Du Bois, *Arch. Intern. Med.*, 17, 863 (1916): $S = W^{0.425} \times H^{0.725} \times 71.84$, or $S = W^{0.425} \times H^{0.725} \times 1.8564$ (S = body surface in cm^2 , W = weight in kg, H = height in cm)

The basal metabolism (or basal metabolic rate, BMR) is the energy requirement of the fasting body, physically and mentally at rest, for 24 hours.

Met

Distributions of various organs to the basal metabolism¹

Organ	Weight (kg)	Proportion of body weight (%)	Oxygen consumption		Proportion of basal metabolism (%)
			per kg (ml/min)	whole organ (ml/min)	
(a) Liver, ...	1.5	2.1	44	66	26.4
(b) Brain, ...	1.4	2.0	33	46	18.3
(c) Heart, ...	0.3	0.43	94	23	9.2
(d) Kidneys, ...	0.3	0.43	61	18	7.2
(a)-(d) together,	153	61.1
(e) Skeletal muscle, ...	27.8	39.7	2.3	64	25.6
Total (a)-(e)	217	86.7

The BMR is dependent on many factors^{2,3}, particularly sex, height and weight, bodily constitution, age and hormonal balance daily and seasonal rhythms as well as climatic effects have also been observed. In women, slight variations occur during the course of the menstrual cycle^{2,4}, and there is an increase of about 20% towards the end of pregnancy⁵. Many standard values for the BMR have been published, in common use are those of HARRIS and BENEDICT⁶, ROOTH⁷, BEARSON and DUNN⁸, ROBERTSON and ANDERSON⁹, and FLETCHER¹⁰. Standard values for children have been published by SNODGRASS¹¹ and by LEWIS et al.¹² The BMR of infants¹³ and children¹² has been extensively investigated and that of the 50-90 year-old group has been the subject of a special study¹⁴.

Standard values of the BMR are usually related to body surface area (for the determination of body surface area see pages 537 and 538), but more recently suggestions have been made to use the fat-free body mass (muscle mass or 'active tissue mass')¹⁵, an accepted measure of which is the urinary creatinine excretion¹⁶. To infants the BMR is best related to body weight¹⁷.

$$RQ = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}$$

Variation of RQ with age¹⁸

Newborn, first hours of life, ...	0.90
first days of life, ...	0.73
end of 1st week, ...	0.82
Adults, postabsorptive (basal RQ), ...	0.82

The following formulae can be used for calculating the BMR (\dot{E} = energy consumption in kilocalories per unit time, \dot{V}_{O_2} = O_2 consumption in litres per unit time, \dot{V}_{CO_2} = CO_2 production in litres per unit time, \dot{H}_N = urinary nitrogen excretion in grammes per unit time):

$$\dot{E} = 4.825 \dot{V}_{O_2} \quad (1)$$

(when only O_2 consumption is measured)

$$\dot{E} = 3.941 \dot{V}_{O_2} + 1.106 \dot{V}_{CO_2} \quad (2a)$$

$$\dot{E} = 3.78 \dot{V}_{O_2} + 1.16 \dot{V}_{CO_2} \quad (2b)$$

(when O_2 consumption and CO_2 production are measured)

$$\dot{E} = 3.941 \dot{V}_{O_2} + 1.106 \dot{V}_{CO_2} - 2.17 \dot{H}_N \quad (3a)$$

$$\dot{E} = 3.78 \dot{V}_{O_2} + 1.16 \dot{V}_{CO_2} - 2.98 \dot{H}_N \quad (3b)$$

(when protein breakdown is also determined)

Formula (1)²⁰ assumes a RQ of 0.82, the caloric values of LOREY were used for formulae (2a) and (3a)²¹, those of RUANZA for formulae (2b) and (3b)²².

Calorific value, oxygen consumption and carbon dioxide production per gramme of protein, fat and carbohydrate burnt in the body and per gramme of nitrogen excreted in the urine²³

	Oxygen consumed (ml/g)	Carbon dioxide produced (ml/g)	RQ	kcal/g		kcal/l	
				from RUANZA	from LOREY	Oxygen	Carbon dioxide
Protein	966.3	773.9	0.801	4.10	4.316	4.485	5.579
Urinary N	5939.0	4757.0	0.801	25.63	26.54	4.485	5.579
Fat	2019.3	1427.3	0.707	9.3	9.461	4.686	6.629
Carbohydrate	828.8	828.8	1.000	4.1	4.182	5.047	5.047

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¹⁸ ERNSTER and LUFY, *Advanc. metab. Disord.*, 1, 95 (1964).

¹⁹ SMITH, C.A., *The Physiology of the Newborn Infant*, 3rd ed., Blackwell, Oxford, 1959, page 203; BEURENDT, 11., *Diagnostic Tests in Infants and Children*, 2nd ed., Lea & Febiger, Philadelphia, 1962, page 33.

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²¹ WEIR, J.B. DE V., *J. Physiol. (Lond.)*, 109, 1 (1949).

²² CONSOLAZIO et al., *Physiological Measurements of Metabolic Functions in* McGraw-Hill, New York, 1963, page 315.

²³ From PETERS and VAN SLYKE, *Quantitative Clinical Chemistry*, 2nd ed., Williams & Wilkins, Baltimore, 1946, page 3.

Standard BMR values

kcal/m ² /h							kJ/m ² /h*						
Age in years	Men			Women			Age in years	Men			Women		
	Standard of Handbook of Biological Data ¹		Standard of FLEISCH ²	Standard of Handbook of Biological Data ¹		Standard of FLEISCH ²		Standard of Handbook of Biological Data ¹		Standard of FLEISCH ²	Standard of Handbook of Biological Data ¹		Stand of FLEISCH
	Mean	95% range	Mean	Mean	95% range	Mean		Mean	95% range	Mean	Mean	95% range	Mea
1	-	-	53.0	-	-	53.0	1	-	-	222	-	-	222
2	-	-	52.4	-	-	52.4	2	-	-	219	-	-	219
3	60.1	51.8-68.3	51.3	54.5	47.0-62.0	51.2	3	252	217-286	215	228	197-260	214
4	57.9	49.9-65.9	50.3	53.9	46.5-61.3	49.8	4	242	209-276	211	226	195-257	208
5	56.3	48.5-64.1	49.3	53.0	45.7-60.3	48.4	5	236	203-268	206	222	191-252	203
6	54.0	46.5-61.5	48.3	51.2	44.1-58.3	47.0	6	226	195-257	202	214	185-244	197
7	52.3	45.1-59.5	47.3	49.7	42.8-56.6	45.4	7	219	189-249	198	208	179-237	190
8	50.8	43.8-57.8	46.3	48.0	41.4-54.6	43.8	8	213	183-242	194	201	173-229	183
9	49.5	42.7-56.3	45.2	46.2	39.8-52.6	42.8	9	207	179-236	189	193	167-220	179
10	47.7	41.1-54.3	44.0	44.9	38.7-51.1	42.5	10	200	172-227	184	188	162-214	178
11	46.5	40.1-52.9	43.0	44.1	38.0-50.2	42.0	11	195	168-221	180	185	159-210	176
12	45.3	39.0-51.6	42.5	42.0	36.2-47.8	41.3	12	190	163-216	178	176	152-200	173
13	44.5	38.4-50.6	42.3	40.5	34.9-46.1	40.3	13	186	161-212	177	170	146-193	169
14	43.8	37.8-49.8	42.1	39.2	33.8-44.6	39.2	14	183	158-208	176	164	141-187	164
15	43.7	37.7-49.7	41.8	38.3	33.0-43.6	37.9	15	182	158-208	175	160	138-182	159
16	42.9	37.0-48.8	41.4	37.7	32.5-42.9	36.9	16	180	155-204	173	158	136-180	154
17	41.9	36.1-47.7	40.8	36.2	31.2-41.2	36.3	17	175	151-200	171	152	131-172	152
18	40.5	34.9-46.1	40.0	35.7	30.8-40.6	35.9	18	170	146-193	167	149	129-170	150
19	40.1	34.6-45.6	39.2	35.4	30.5-40.3	35.5	19	168	145-191	164	148	128-169	149
20	39.8	34.3-45.3	38.6	35.3	30.4-40.2	35.3	20	167	144-190	162	148	127-168	148
21	39.4	34.0-44.8	-	35.2	30.3-40.1	-	21	165	142-188	-	147	127-168	-
22	39.2	33.8-44.6	-	35.2	30.3-40.1	-	22	164	141-187	-	147	127-168	-
23	39.0	33.6-44.4	-	35.2	30.3-40.1	-	23	163	141-186	-	147	127-168	-
24	38.7	33.4-44.0	-	35.1	30.3-39.9	-	24	162	140-184	-	147	127-167	-
25	38.4	33.1-43.7	37.5	35.1	30.3-39.9	35.2	25	161	139-183	157	147	127-167	147
26	38.2	32.9-43.5	-	35.0	30.2-39.8	-	26	160	138-182	-	146	126-167	-
27	38.0	32.8-43.2	-	35.0	30.2-39.8	-	27	159	137-181	-	146	126-167	-
28	37.8	32.6-43.0	-	35.0	30.2-39.8	-	28	158	136-180	-	146	126-167	-
29	37.7	32.5-42.9	-	35.0	30.2-39.8	-	29	158	136-180	-	146	126-167	-
30	37.6	32.4-42.8	36.8	35.0	30.2-39.8	35.1	30	157	136-179	154	146	126-167	147
31	37.4	32.2-42.6	-	35.0	30.2-39.8	-	31	157	135-178	-	146	126-167	-
32	37.2	32.1-42.3	-	34.9	30.1-39.7	-	32	156	134-177	-	146	126-166	-
33	37.1	32.0-42.2	-	34.9	30.1-39.7	-	33	155	134-177	-	146	126-166	-
34	37.0	31.9-42.1	-	34.9	30.1-39.7	-	34	155	134-176	-	146	126-166	-
35	36.9	31.8-42.0	36.5	34.8	30.0-39.6	35.0	35	154	133-176	153	146	126-166	146
36	36.8	31.7-41.9	-	34.7	29.9-39.5	-	36	154	133-175	-	145	125-165	-
37	36.7	31.6-41.8	-	34.6	29.8-39.4	-	37	154	132-175	-	145	125-165	-
38	36.7	31.6-41.8	-	34.5	29.7-39.3	-	38	154	132-175	-	144	124-164	-
39	36.6	31.5-41.7	-	34.4	29.7-39.1	-	39	153	132-175	-	144	124-164	-
40	36.5	31.5-41.5	36.3	34.3	29.6-39.0	34.9	40	153	132-174	152	144	124-163	146
45	36.3	31.3-41.3	36.2	33.9	29.2-38.6	34.5	45	152	131-173	152	142	122-162	144
50	36.0	31.0-40.0	35.8	33.4	28.8-38.0	33.9	50	151	130-167	150	140	121-159	142
55	35.4	30.5-40.3	35.4	32.9	28.4-37.4	33.3	55	148	128-169	148	138	119-157	139
60	34.8	30.0-39.6	34.9	32.4	27.9-36.9	32.7	60	146	126-166	146	136	117-154	137
65	34.0	29.3-38.7	34.4	31.8	27.4-36.2	32.2	65	142	123-162	144	133	115-152	135
70	33.1	28.5-37.7	33.8	31.3	27.0-35.6	31.7	70	139	119-158	141	131	113-149	133
75	31.8	27.4-36.2	33.2	31.1	26.8-35.4	31.3	75	133	115-152	139	130	112-148	131
and over							and over						

* The values in kJ have been calculated by using the relationship 1 kcal₁₅ = 4.1855 kJ (see page 213).

¹ BOOTHBY and DuBois, in ALBRITTON, E.C. (Ed.), *Standard Values in Nutrition and Metabolism*, Saunders, Philadelphia, 1954, page 241. The values are based on 4016 measurements. The normal range has been calculated

using a mean coefficient of variation of 6.9. The following data were used: Mayo Foundation Standards of BOOTHBY, BERKSON and DUNN; standard of ROBERTSON and REID; Carnegie Nutrition Laboratory Standards of HARRISON and BENEDICT.

² FLEISCH, A., *Helv. med. Acta*, 18, 23 (1951). Values based on 24 reports in the literature.

Respiration

(For references see page 546)

symbols used in respiratory physiology¹

1. Gas phase

a) Primary symbols (italic capitals)

(A point over a symbol indicates a time derivative, a bar a mean value)

- V Gas volume
- \dot{V} Gas volume per unit time
- P Gas pressure (partial pressure)
- \bar{P} Mean gas pressure
- F Fractional concentration in dry gas phase
- f Respiratory frequency (breaths per unit time)
- D Diffusing capacity

(b) Secondary symbols (small italic capitals) and abbreviations (small upright capitals)

- i Inspired gas
- e Expired gas
- A Alveolar gas
- D Dead-space gas
- T Tidal gas

- B Barometric pressure
- $STPD$ Standard temperature and pressure, dry (gas at 760 mm Hg, dry)
- $BTPS$ Body temperature and pressure, saturated with vapour (gas at 37°C, measured barometric pressure)
- $ATPS$ Ambient temperature and pressure, saturated (ambient temperature and pressure, saturated with vapour)

2. Blood phase

(a) Primary symbols (italic capitals)

- Q Blood volume
- \dot{Q} Blood volume per unit time
- S O₂ or CO₂ saturation of haemoglobin (as percent; O₂ or CO₂ capacity)

(b) Secondary symbols (italic small letters)

- a Arterial blood
- v Venous blood
- c Capillary blood

Respiratory variable	Definition	Unit	Remarks, normal values
Lung volumes and capacities	<p><i>Subdivisions of the lung volume¹</i></p>		
	The subdivisions on the right apply to all levels of respiratory effort and do not overlap. The capacities on the left include two or more of the primary subdivisions		All volumes to be corrected to BTPS (also page 269). Measurements are usually made on the recumbent patient; rat higher values are obtained if the patient sitting or standing ²
<i>Tidal volume (V_T)</i>	The volume of air inspired and expired at each breath	l	For normal values see Table 1, page 55
<i>Inspiratory reserve volume (IRV)</i>	The maximum volume of air that can be additionally inspired after a normal inspiration	l	
<i>Expiratory reserve volume (ERV)</i>	The maximum volume of air that can be additionally expired after a normal expiration	l	For normal values see Table 2, page 55

Respiration

(For references see page 546)

Respiratory variable	Definition	Unit	Remarks, normal values
<i>Residual volume (RV)</i>	The volume of air remaining in the lungs after a maximum expiration	l	For normal values see Tables 2, 3 and 5, pages 550–551
<i>Total lung capacity (TLC)</i>	The volume of air contained in the lungs after a maximum inspiration	l	For normal values see Table 2, page 550, and Table 5, page 551. For determination in children see Figure 1, page 547. The total lung capacity can be calculated from the normal vital capacity as follows ² : $\left. \begin{array}{l} 15-34 \text{ years } 0.8 \\ 35-49 \text{ years } 0.75 \\ > 50 \text{ years } 0.65 \end{array} \right\} \times \text{vital capacity}$
<i>Vital capacity (VC)</i>	The maximum volume of air that can be forcibly inspired after a maximum expiration (inspiratory vital capacity) or that can be forcibly expired after a maximum inspiration (expiratory vital capacity)	l	It is better to measure the inspiratory VC since this is reproducible even in diseased persons, whereas the expiratory VC may fluctuate as a result of the check-valve mechanism. For normal values see Table 2, page 550, and Tables 3–5, page 551. For measurement in ambulant or bedded patients with healthy lungs see Figures 3 and 4, page 547. The 'crying' VC of the newborn is about 0.14 l ⁴
<i>Inspiratory capacity (IC)</i>	The maximum volume of air that can be inspired from the resting expiratory level	l	For normal values see Table 2, page 550
<i>Functional residual capacity (FRC)</i>	The volume of air in the lungs at the resting expiratory level	l	For normal values see Table 2, page 550. For determination in children see Figure 2, page 547. The FRC of the newborn is about 70 ml ⁴
Ventilation			
<i>Minute ventilation (\dot{V}_T)</i>	The volume of air inspired or expired in one minute	l min ⁻¹	Since the respiratory quotient in normal breathing at rest is less than 1, the inspiratory minute ventilation differs from the expiratory minute ventilation. The amount of the minute volume is a function mainly of the energy consumption of the body, the dead-space ventilation and the respiratory frequency, and is thus subject to large individual variations. For calculation of the normal value see ROSSIER et al. ⁵ . For normal measured values see Table 1, page 550
<i>Alveolar ventilation (\dot{V}_A)</i>	The volume of air entering the alveoli per minute, or the amount of alveolar air expired per minute	l min ⁻¹	In a young man weighing 70 kg with an O_2 intake of 250 ml/min the alveolar ventilation must be at least 4.3 l/min if arterialization is to be complete ³ . The alveolar ventilation is calculated by means of BOHR's alveolar equation. The normal value is affected by postural changes and under resting conditions is 70–80%, under heavy loading about 85%, of the total ventilation; the remainder is the dead-space ventilation, or functional dead space ^{5, 6}

Respiration

(For references see page 546)

Respiratory variable	Definition	Unit	Remarks, normal values
<i>Respiratory time quotient</i>	Ratio of the time of expiration to the time of inspiration		For normal values see Table 1, page 550
<i>Mixing time</i>	The time required for stabilization of the gas concentration in the lung-spirometer system		The time required for stabilization of the gas concentration in the lung-spirometer system. Mixing is normally complete after 2-3 min. For helium methods see BRISCOE ⁷
Tests of ventilatory function			
<i>Maximum voluntary ventilation (VV_{max}), maximum breathing capacity (RC)</i>	The maximum minute ventilation attainable by voluntary hyperventilation	l min ⁻¹	Calculated from the value measured over 120 s. The value is expressed as a percentage of the maximum voluntary ventilation × 37, or normal vital capacity × 30. For normal values in adults see Figure 6, page 548. For values used in the evaluation of permanent impairment see the literature ¹⁰
<i>Forced expiratory volume (FEV₁)</i>	The volume of air expired per unit time during forced expiration following full inspiration	l	For normal values in adults see the literature ^{10, 11}
<i>Forced expiratory volume (FEV₁)</i>	The forced expiratory volume expressed as percentage of the vital capacity 100 FEV ₁ /VC	%	For normal values see Table 5, page 551, and Figure 8, page 549
<i>Maximum expiratory flow rate (MEFR), peak flow rate</i>	The flow rate at a particular point during forced expiration	l s ⁻¹	For normal values in adults see Table 5, page 551, and Figure 8, page 549
<i>Maximum inspiratory flow rate (MIFR)</i>	The flow rate at a particular point during forced inspiration	l s ⁻¹	
<i>Maximum mid-expiratory flow (MMF)</i>	The flow rate during the middle half of a forced expiration	l s ⁻¹	For normal values in adults see Figure 9, page 549
Pulmonary circulation			
<i>Intra-arterial pressure</i>	The ratio of the blood pressure in any part of the blood vessel to the atmospheric pressure	mm Hg	For normal values see page 553

Respiratory variable	Definition	Unit	Remarks, normal values
<i>expiratory time quotient</i>	Ratio of the time of expiration to the time of inspiration		For normal values see Table 1, page 550
<i>living time</i>	The time required for stabilization of the gas concentration in the lung-spirometer system		For normal values see Table 1, page 550 see BRISCOM?

Tests of ventilatory function

<i>Maximum voluntary ventilation (MVV), maximum breathing capacity (MBC)</i>	The maximum minute ventilation attainable by voluntary hyperventilation	$l \cdot \text{min}^{-1}$	Calculated from the value measured over 10-20 s. For determination from age and respiratory frequency see Figure 5, page 548. Normal value at a respiratory frequency of $50/\text{min}$ is 37 , or normal vital capacity $\times 30$. For normal values in adults see Figure 6, page 548. For values used in the evaluation of permanent impairment see the literature! ¹⁰
<i>Forced expiratory volume (FEV₁)</i>	The volume of air expired per unit time during forced expiration following full inspiration	l	For normal values in the USA and USA see the literature! ^{10, 11}
<i>Percentage forced expiratory volume</i>	The forced expiratory volume expressed as percentage of the vital capacity $100 \text{ FEV}_1/\text{VC}$	%	For normal values see Table 5, page 551, and Figure 8, page 549
<i>Maximum expiratory flow rate (MEFR), peak flow rate</i>	The flow rate at a particular point during forced expiration	$l \cdot s^{-1}$	For normal values see Table 5, page 551, and Figure 8, page 549
<i>Maximum inspiratory flow rate (MIFR)</i>	The flow rate at a particular point during forced inspiration	$l \cdot s^{-1}$	For normal values see Table 5, page 551, and Figure 8, page 549
<i>Maximum mid-expiratory flow (MMEF)</i>	The flow rate during the middle half of a forced expiration	$l \cdot s^{-1}$	For normal values in adults see Figure 9, page 549

Pulmonary circulation

<i>Intravascular pressure</i>	The ratio of the blood pressure in any part of the blood vessel to the atmospheric pressure	mm Hg	For normal values see page 553
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Respiration

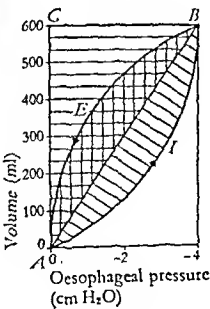
(For references see page 546)

Respiratory variable	Definition	Unit	Remarks, normal values
<i>Transmural pressure</i>	The difference between the blood pressure in the vessel and the external pressure on the vessel	mm Hg	The pressure acting externally on the monary arteries and veins is equal to intrathoracic pressure
<i>Driving pressure</i>	The pressure difference between the two ends of any section of a blood vessel	mm Hg	
<i>Vascular resistance</i>	Ratio of the driving pressure in the pulmonary circulation to the minute volume	dyn s cm ⁻⁵	
<i>Minute volume</i>	The volume of blood passing through the lungs in one minute	l min ⁻¹	Obtained by using Fick's principle, according to which the minute volume is equal to the ratio $\frac{\text{O}_2 \text{ intake (ml/min)}}{\text{arteriovenous O}_2 \text{ difference (ml/l)}}$ In resting adults the blood flow through lungs is about 5 l/min
<i>Intrapulmonary blood volume</i>	The volume of blood contained between the origin of the pulmonary artery and the junction of the pulmonary veins with the left atrium	l	Normal value in adults about 900 ml. volume of blood contained in the pulmonary capillaries in resting adults is 75 ml ¹² . For normal values in children BUCCI ¹²
<i>Ventilation/perfusion ratio (\dot{V}_A/\dot{Q})</i>	Ratio of the alveolar ventilation to the blood flow in the capillaries (perfusion)		In resting adults the alveolar ventilation about 4 l/min and the blood flow about 5 l/min, so that the ventilation/perfusion ratio is about 0.8
<i>Intrapulmonary shunt volume</i>	Proportion of venous blood in the blood flowing through the aorta	vol%	Physiologically, the venous blood present derives from the bronchial venous blood flowing into the pulmonary veins, from intrapulmonary arteriovenous shunts, and to a lesser extent from coronary venous blood entering via the veins of THEBES and via communications between the pulmonary and pulmonary veins and the mediastinal and pulmonary veins. Normal value young adults at rest 2 (0-4)% ¹³
Blood gases and diffusion	The pressures given are partial pressures (the partial pressure of a component of a gas mixture is the pressure it would exert if it alone occupied the whole volume of the mixture). The pressure of an (ideal) gas mixture is equal to the sum of the partial pressures of its components		Most types of gas analysis apparatus give so-called dry percentages of the gases, expressed as fractions F of the dry gas mixture. The pressure P of a component gas (mm Hg) in the original mixture is given $P_{\text{gas}} = F_{\text{gas}} (B - P_{\text{H}_2\text{O}}),$ where B = barometric pressure (mm Hg) $P_{\text{H}_2\text{O}} = 47$ mm Hg at 37 °C
<i>Alveolar O₂ pressure ($P_{A\text{O}_2}$)</i>		mm Hg	Adults ⁹ : 100 (95-105) mm Hg
<i>Alveolar CO₂ pressure ($P_{A\text{CO}_2}$)</i>		mm Hg	Adults ⁹ : 40 (38-42) mm Hg
<i>Arterial O₂ saturation ($S_{a\text{O}_2}$)</i>		%	Adults ⁹ : 97 (95-99)%. See also page 576
<i>Arterial O₂ pressure ($P_{a\text{O}_2}$)</i>		mm Hg	Adults ⁹ : 80-100 mm Hg. See also page 57

Respiratory variable	Definition	Unit	Remarks, normal values
arterial CO_2 pressure ($P_{a\text{CO}_2}$)		mm Hg	Adults*: 40 (38–42) mm Hg. See also page 570
arterial pH value			Adults*: 7.4 (7.36–7.44) See also page 560
diffusing capacity (D_L)	The rate at which a gas passes from the alveoli into the blood at a partial-pressure difference of 1 mm Hg	ml min^{-1} mm Hg $^{-1}$	<p>Measured by using CO or O_2. The diffusing capacity is affected by constitution, age, lung volume, metabolic state and posture. For normal values in the lung itself (D_L) see Table 7, page 552. The value for CO is</p> $\frac{1}{D_L} = \frac{1}{D_M} + \frac{1}{\delta V_c}$ <p>where δ is a velocity constant (dependent on P_{O_2}). V_c the volume of blood in the capillaries</p>
Difference between alveolar and arterial partial pressure of O_2	$P_{a\text{O}_2} - P_{a\text{O}_2}$	mm Hg	<p>constitutes the arterial blood), (2) the non-uniformity of the ventilation-perfusion process in the different parts of the lung (even in healthy persons ventilation is in excess of perfusion or vice versa in some alveoli), and (3) the fall in partial pressure due to perfusion (of little consequence in healthy persons under normal conditions). The difficulty of calculating the last factor precisely is the reason for the wide fluctuations in published data on the diffusing capacity of the lungs for O_2</p>

Respiratory mechanics

Compliance (C)	The expansibility of the lungs and/or thorax expressed as the volume change per unit pressure change	$\text{l cm H}_2\text{O}^{-1}$	<p>Normal values in young men³</p> <p>Compliance of the lungs (C_L) about 0.21 $\text{cm H}_2\text{O}^{-1}$</p> <p>Compliance of the thorax (C_T) about 0.21 $\text{cm H}_2\text{O}^{-1}$</p> <p>Compliance of the lungs + thorax (C_{L+T}) about 0.11 $\text{cm H}_2\text{O}^{-1}$</p> <p>where $\frac{1}{C_{L+T}} = \frac{1}{C_L} + \frac{1}{C_T}$</p> <p>Compliance of the lungs in the newborn⁴ 5 $\text{ml cm H}_2\text{O}^{-1}$</p> <p>Compliance of the lungs in children: see Figure 11, page 549</p> <p>Compliance of the lungs in adults: see Table 9, page 552</p>
Specific compliance	The ratio of compliance to functional residual capacity		<p>Pet litre of functional residual capacity⁵</p> <p>Adults 0.05–0.06 l $\text{cm H}_2\text{O}^{-1}$</p> <p>Newborn 0.065 l $\text{cm H}_2\text{O}^{-1}$</p>
Elastance	Reciprocal of the compliance	$\text{cm H}_2\text{O l}^{-1}$	A measure of the elastic resistance of the lungs and thorax

Respiratory variable	Definition	Unit	Remarks, normal values
<i>Nonelastic (viscous) resistances</i>	Expressed as the pressure difference corresponding to unit ventilation	$\text{cm H}_2\text{O s l}^{-1}$	
<i>Airway resistance</i>	Resistance to flow in the airways		Can be measured by means of the body plethysmograph, usually with rapid superficial breathing (frequency 200/min). For normal values see Table 8, page 552. For values at normal respiratory frequency see JAEGER and OTIS ¹⁴
<i>Pulmonary tissue resistance</i>	Frictional and deformational resistance of the pulmonary tissue		Obtained as the difference between the pulmonary total and airway resistances. For normal values see Table 8, page 552
<i>Total pulmonary resistance</i>	Airway resistance plus tissue resistance		Determined by measuring the intrathoracic or oesophageal pressure. In healthy younger subjects about 20% is tissue resistance and about 80% airway resistance. For normal values in children see Figure 12, page 549, in adults Table 8, page 552
<i>Thoracic tissue resistance</i>	Deformational resistance of the thoracic tissue		Obtained approximately as the difference between the total respiratory and total pulmonary resistances
<i>Total (nonelastic) respiratory resistance</i>	Total pulmonary resistance plus thoracic tissue resistance		Can be measured approximately by means of a pneumotachograph. Exact values can be obtained only by using a respirator ('iron lung') with complete relaxation of the muscles involved in respiration
<i>Conductance</i>	Reciprocal of the nonelastic resistance	$\text{l s}^{-1} \text{cm H}_2\text{O}^{-1}$	
<i>Work of breathing (A)</i>	<p>The work required to overcome the elastic and non-elastic resistances of the lungs and thorax and the airway resistance:</p> <p>$A = \text{force} \times \text{distance}$ $= \text{pressure} \times \text{volume}$</p>	m kg or l atm	The total work of breathing can be precisely determined only by having the subject breathe passively in a respirator and measuring the pressures required for various minute ventilations. For a tidal volume of 500 ml and respiratory frequency of 15/min this method gives a total work of breathing of $0.315 \text{ kg m min}^{-1}$ ¹⁵ . By ignoring the work required to overcome the thoracic tissue resistance, the work of breathing can be obtained from the respiratory loop (see the adjacent diagram). It is the sum of the products of the forces (measurable as pressures in the oesophagus) and corresponding tidal volumes. The respiratory loop can be calculated from the pneumotachogram and pressure curve or registered by means of a cathode-ray oscillograph or other directly recording instrument. For normal values of the components of the work of breathing for a single breath see Table 10, page 552
<p><i>Volume-pressure diagram for a single breath (respiratory loop)¹⁶</i></p>  <p>Area AIBC Total work done against the elastic and nonelastic resistances of the pulmonary tissue and the airway resistance</p> <p>Area AIB Work done against the nonelastic resistance of the pulmonary tissue and the airway resistance during inspiration</p> <p>Area ABC Work done against the elastic resistance of the pulmonary tissue during inspiration</p> <p>Area BEA Work done against the nonelastic resistance of the pulmonary tissue and the airway resistance during expiration. Expiration does not require active work but takes place passively through the elastic contraction of the lung expanded during inspiration</p>			
<p>References</p> <p>¹ PAPPENHEIMER et al., <i>Fed. Proc.</i>, 9, 602 (1950). ² WHITFIELD et al., <i>Brit. J. soc. Med.</i>, 4, 86 (1950); HAMM and KLEINSORG, <i>Dtsch. Arch. klin. Med.</i>, 203, 234 (1956); MORENO and LYONS, <i>J. appl. Physiol.</i>, 16, 27 (1961); GEUBELLE and GOFFIN, <i>Acta paediat. (Uppsala)</i>, 51, 255 (1962). ³ COMROE et al., <i>The Lung</i>, 2nd ed., Year Book Medical Publishers, Chicago, 1962. ⁴ COOK et al., <i>Advanc. Pediat.</i>, 11, 11 (1960). ⁵ ROSSIER et al., <i>Physiologie und Pathophysiologie der Atmung</i>, 2nd ed., Springer, Berlin, 1958. ⁶ FRUHMANN and STURM, <i>Z. ges. exp. Med.</i>, 139, 357 (1965). ⁷ BRISCOE, W. A., <i>Clin. Sci.</i>, 11, 45 (1952). ⁸ BUEHMANN et al., <i>Schweiz. med. Wschr.</i>, 91, 105 (1961). ⁹ HERTZ, C. W., <i>Internist (Berl.)</i>, 1, 80 (1960). ¹⁰ Committee on Rating of Mental and Physical Impairment, <i>J. Amer. med. Ass.</i>, 194, 919 (1965). ¹¹ COTLÉ et al., <i>Brit. med. J.</i>, 1, 1016 (1966). ¹² BUCCI et al., <i>J. Pediat.</i>, 58, 820 (1961). ¹³ FRUHMANN, G., <i>Z. ges. exp. Med.</i>, 139, 391 (1965). ¹⁴ JAEGER and OTIS, <i>J. appl. Physiol.</i>, 19, 813 (1964). ¹⁵ OTIS et al., <i>J. appl. Physiol.</i>, 2, 592 (1950); OTIS, A. B., <i>Physiol. Rev.</i>, 34, 449 (1954). ¹⁶ HAMM et al., <i>Z. klin. Med.</i>, 157, 133 (1962).</p>			

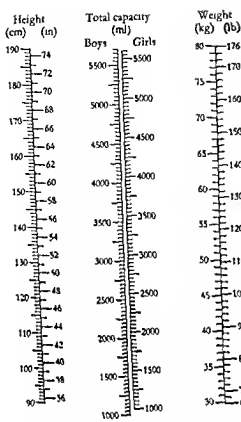


Fig. 1. Determination of total lung capacity in children (from LYONS and TANNER, *J appl. Physiol.*, 17, 601 [1962])

Fig. 2. Determination of functional residual capacity in children (from LYONS and TANNER, *J appl. Physiol.*, 17, 601 [1962])

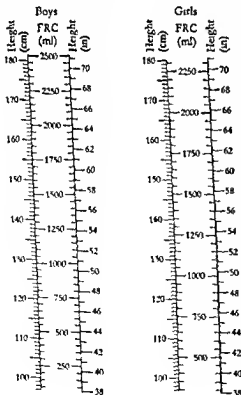


Fig. 3. Determination of vital capacity in healthy adults (from MILLER et al., *J. appl. Physiol.*, 14, 157 [1959])

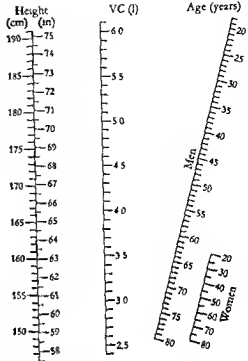
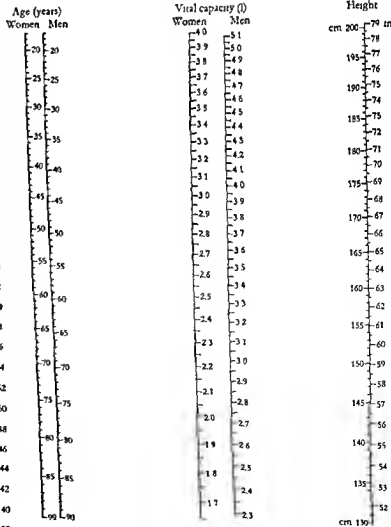


Fig. 4. Determination of vital capacity in recumbent healthy adults (from BALDWIN et al., *Medicine [Baltimore]*, 27, 243 [1948])



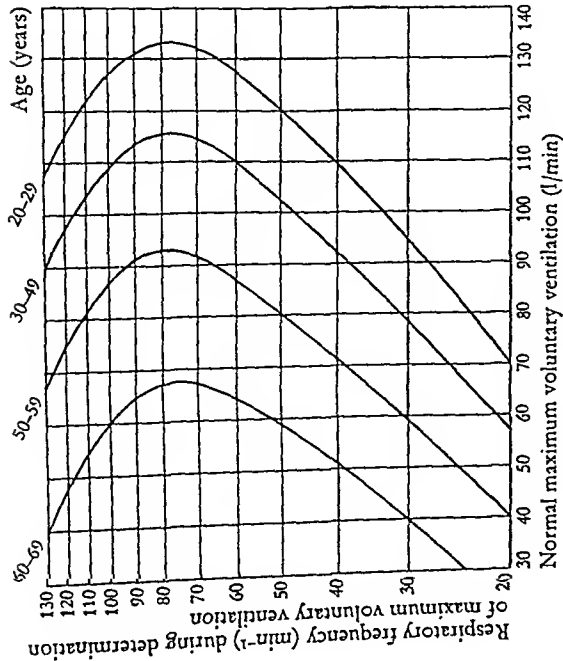


Fig. 5. Determination of maximum voluntary ventilation as a function of respiratory frequency (from FRUHMANN and ZIEGLER, *Z. klin. Med.*, 157, 586 [1963])

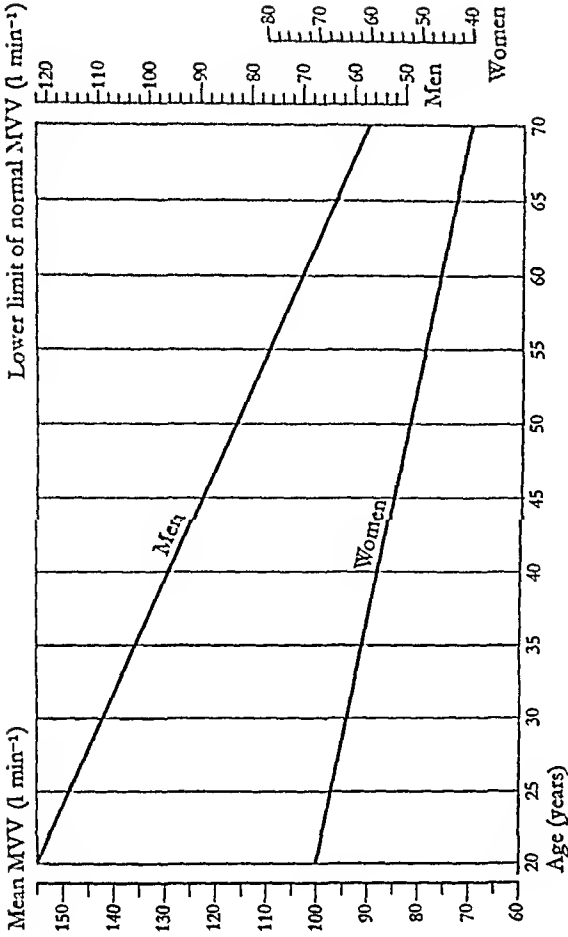


Fig. 6. Determination of maximum voluntary ventilation (MVV) in adults (respiratory frequency 40/min) (from BIRATH et al., *Acta med. scand.*, 173, 193 [1963])

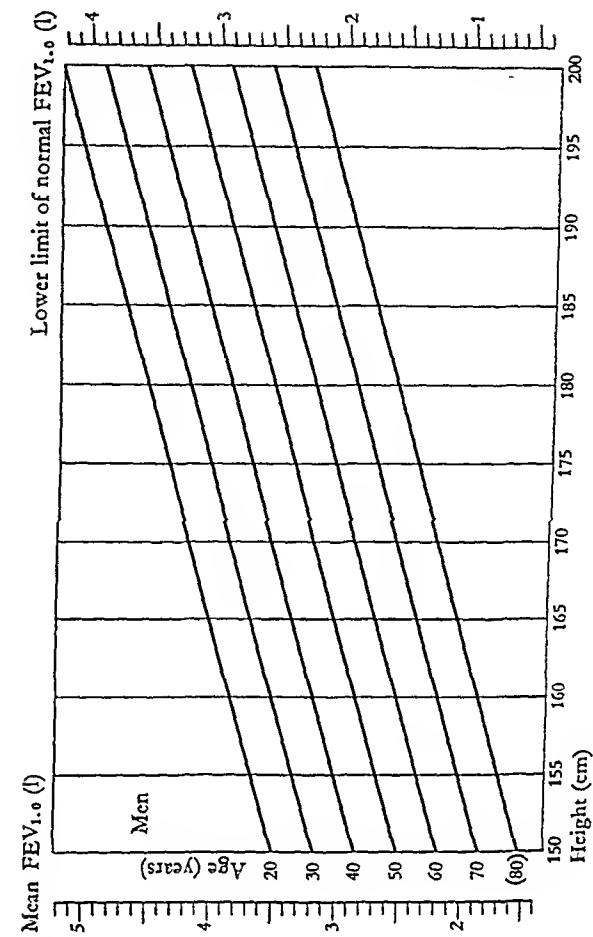
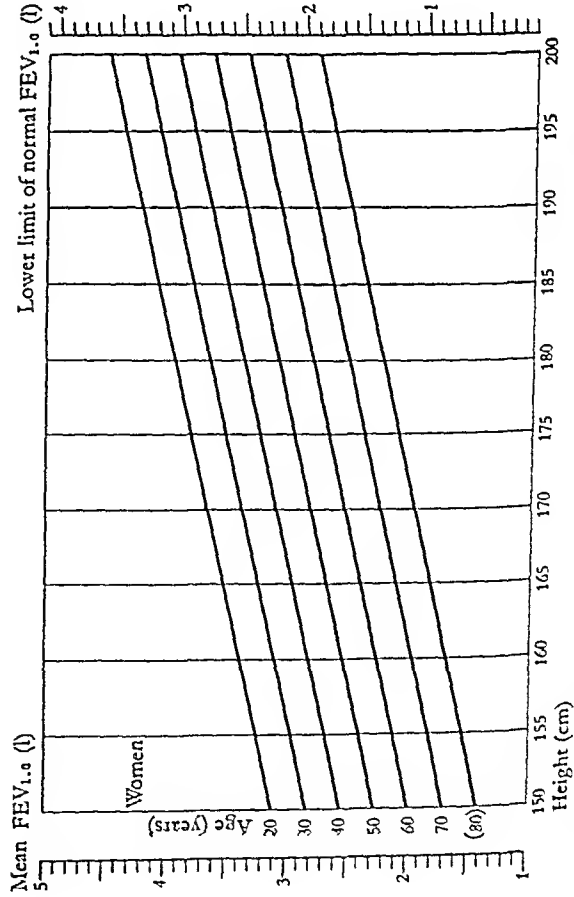


Fig. 7. Determination of forced expiratory volume (FEV_{1.0}) in adults (from BERGLUND et al., *Acta med. scand.*, 173, 185 [1963])

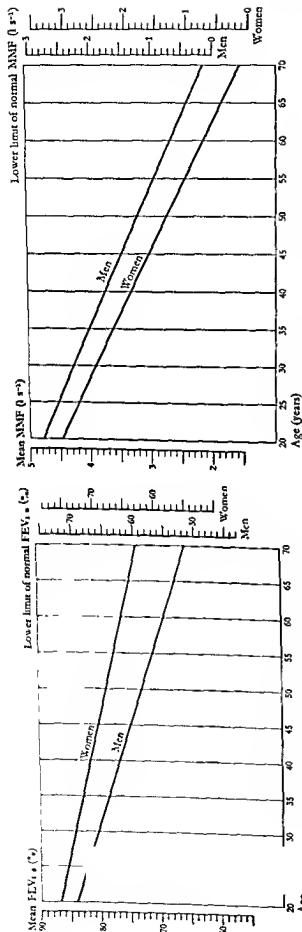


Fig. 8. Determination of percentage forced expiratory volume (FEV_{1.0}) in adults (from BEAGLIOU *et al.*, *Acta med scand.*, 172, 185 [1963])

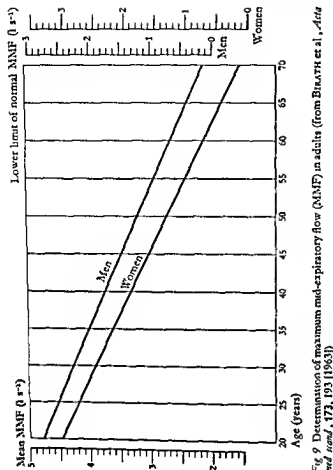


Fig. 9. Determination of maximum mid-expiratory flow (MMF) in adults (from BYLATH *et al.*, *Acta med scand.*, 173, 193 [1963])

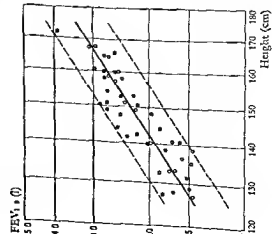


Fig. 10

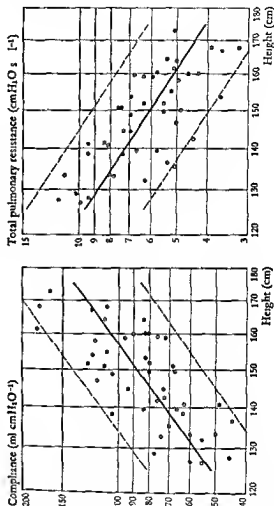


Fig. 11

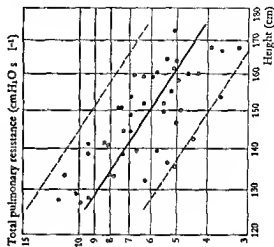


Fig. 12

Fig. 10-12. Determination of forced expiratory volume (FEV_{1.0}), compliance and total pulmonary resistance in children (from BYLATH *et al.*, *Acta paediat.* [Uppsala], 51, 68 [1962])

● Boys
○ Girls
— Regression line
--- 95% confidence limits

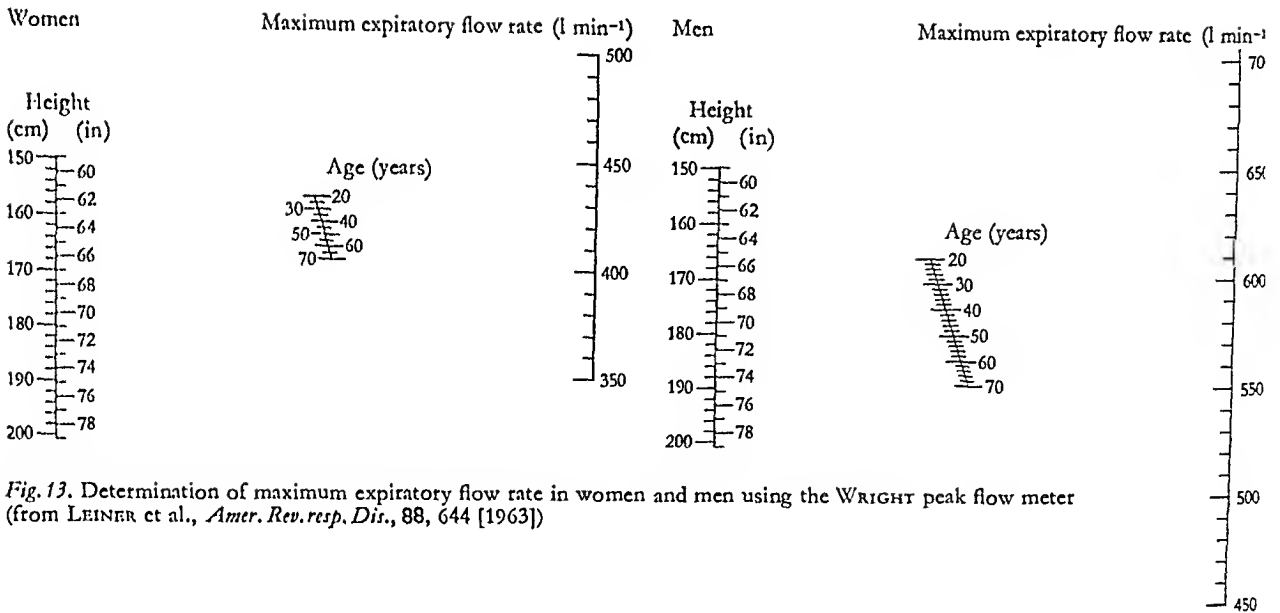


Fig. 13. Determination of maximum expiratory flow rate in women and men using the WRIGHT peak flow meter (from LEINER et al., *Amer. Rev. resp. Dis.*, 88, 644 [1963])

Table 1 Respiratory frequency, tidal volume, minute ventilation and respiratory time quotient in children and adults*

	Respiratory frequency (min ⁻¹)		Tidal volume (ml)		Minute ventilation (l min ⁻¹)		Respiratory time quotient		Reference
	Mean	95% range (extreme range in brackets)	Mean	95% range (extreme range in brackets)	Mean	95% range (extreme range in brackets)	Mean	95% range (extreme range in brackets)	
Newborn, 4-6 days	49.7	(28.0-69.0)	17.3	(9.5-25.9)	0.83	(0.50-1.48)	1.29	(0.97-2.09)	¹
Infants, 11 weeks	62.8	(40.0-87.0)	17.5	(11.0-28.1)	1.03	(0.75-1.37)	1.27	(1.09-1.58)	¹
Children, 2-3 years	23.7	(18.9-30.3)	122	(77-149)	2.8	(2.3-4.0)	1.46	(0.92-1.79)	¹
Children, 4-5 years	23.2	(11.3-30.2)	138	(147-275)	4.0	(3.1-4.7)	1.43	(1.27-1.55)	¹
Children, 6-7 years	21.1	(17.4-24.0)	203	(180-223)	4.3	(3.7-4.9)	1.60	(1.15-2.52)	¹
Boys, 12 years	16.3	7.9-24.7	305	185-425	4.8	3.7-5.8	-	-	²
Girls, 12 years	16.1	9.8-22.4	289	189-389	4.5	3.1-6.0	-	-	²
Boys, 14 years	17.0	12.8-21.2	316	196-436	5.3	3.8-6.8	-	-	²
Girls, 14 years	15.6	11.4-19.8	315	235-395	4.9	3.6-6.1	-	-	²
Boys, 16 years	15.6	9.3-21.9	344	184-504	5.1	3.4-6.8	-	-	²
Girls, 16 years	15.2	8.9-21.5	282	162-402	4.2	2.5-5.9	-	-	²
Adults, 20-39 years	17.2	-	-	-	8.5	2.5-14.5	1.35	0.79-1.91	³
Adults, 40-59 years	16.9	-	-	-	9.5	-	1.33	0.85-1.81	³
Adults, 60 years and over	16.3	-	-	-	10.5	-	1.54	0.98-2.10	³
Men, resting	11.7	(10.1-13.1)	630	-	7.4	(5.8-10.3)	-	-	⁴
Men, light work (500 m kg min ⁻¹)	17.1	(15.7-18.2)	1670	-	28.6	(27.3-30.9)	-	-	⁴
Men, heavy work (800 m kg min ⁻¹)	21.2	(18.6-23.3)	2030	-	43	(39-45)	-	-	⁴
Women, resting	11.7	-	390	-	4.6	-	-	-	⁴
Women, light work (300 m kg min ⁻¹)	19.0	-	860	-	16.4	-	-	-	⁴

¹ BLÖMER and HAHN, *Z. Kinderheilk.*, 87, 466 (1963).

² SHOCK, N.W., in DITTMER and GREBE (Eds.), *Handbook of Respiration*, Saunders, Philadelphia, 1958, page 44.

³ FRUHMANN, G., *Z. exp. Med.*, 138, 1 (1964).

⁴ TAYLOR, C., *Amer. J. Physiol.*, 135, 27 (1941).

* At rest unless otherwise stated.

Table 2 Lung volumes and capacities in resting adults

	50 young men ¹ (recumbent)		50 young women ¹ (recumbent)		11 men over 50 years ² (semi-recumbent)			50 young men ¹ (recumbent)		50 young women ¹ (recumbent)		11 men over 50 years ² (semi-recumbent)	
	Mean	s	Mean	s	Mean	s		Mean	s	Mean	s	Mean	s
Age (years)	22.9	3.3	23.1	3.4	61.5	6.8	Residual volume (l)	1.19	0.35	1.10	0.30	2.43	0.50
Height (in and cm)	69.3	2.0	64.3	1.7	66.3	1.9	Functional residual capacity (l)	2.18	0.50	1.82	0.39	3.44	0.74
Weight (lb and kg)	176.2	5.1	163.4	4.2	169.0	4.8	Total capacity (l)	5.97	0.81	4.24	0.57	5.92	0.57
Inspiratory capacity (l)	159.5	24.7	126.2	20.4	145.2	27.4	Relative residual capacity (% of total capacity)	19.8	4.4	25.9	5.0	40.9	7.1
Expiratory reserve volume (l)	72.5	11.2	57.2	9.4	65.9	12.4							
Vital capacity (l)	3.79	0.52	2.42	0.36	2.61	0.61							
	0.98	0.26	0.73	0.19	1.01	0.38							
	4.78	0.59	3.14	0.41	3.48	0.48							

¹ From KALTREIDER et al., *Amer. Rev. Tuberc.*, 37, 662 (1938).

² From GREIFENSTEIN et al., *J. appl. Physiol.*, 4, 641 (1952).

Table 3 Residual volume and vital capacity as functions of age¹

Age (years)	Number	Vital capacity (ml)		Residual volume (ml)		Residual volume as percentage of total lung capacity (%)		Age (years)	Number	Vital capacity (ml)		Residual volume (ml)		Residual volume as percentage of total lung capacity (%)	
		Mean	s	Mean	s	Mean	s			Mean	s	Mean	s	Mean	s
Men								Women							
9-13	16	2690	520	540	180	17.3	4.3	14-19	2-3	3330	(300)	820	(220)	19.5	(5.0)
14-19	9-10	4030	540	830	340	17.2	4.3	20-29	9-11	3600	390	1290	340	25.7	6.2
20-29	20-26	5440	720	1410	310	20.6	4.0	30-39	3	3460	(380)	1310	(280)	28.0	(5.0)
30-39	15-19	5030	700	1510	360	22.2	4.0	40-49	3-4	3680	(710)	1390	(490)	30.0	(8.7)
40-49	14-17	4530	500	1690	410	26.8	5.2	50-59	4	3250	(370)	1300	(360)	28.8	(4.6)
50-59	18	4650	970	1740	380	27.8	4.4	60-64	2-3	3140	(400)	1200	(280)	29.5	(4.6)
60-75	7-11	3860	810	1760	330	33.9	5.2								

¹ From ZEMDNER, H., *Hals und Atm.*, 27, 245 (1960)Table 4 Vital capacity in children as a function of age and sex²

Age (years)	Number	Height		Vital capacity (ml)*			Age (years)	Number	Height		Vital capacity (ml)*		
		(in)	(cm)	Mean	s	Extreme range			(in)	(cm)	Mean	s	Extreme range
Boys							Girls						
4	6	40.7	103.4	855	-	540-970	5	9	37.5	95.4	717	-	380-920
5	20	42.0	106.8	1001	-	650-1240	6	26	41.9	106.4	959	-	650-1300
6	62	44.2	112.2	1246	197	860-1730	7	62	43.8	111.5	1172	176	760-1730
7	112	46.0	116.9	1393	210	970-2380	8	81	45.0	114.4	1326	196	970-1940
8	98	47.9	121.8	1585	238	1130-2270	9	76	47.6	121.0	1513	215	860-2100
9	110	51.1	129.9	1852	266	1300-2480	10	73	50.0	127.0	1634	247	1080-2430
10	87	52.5	133.4	2022	283	1510-2860	11	117	52.0	132.1	1806	295	970-2590
11	113	54.2	137.8	2150	292	1400-3020	12	119	53.4	135.9	1943	260	1350-2750
12	114	56.1	142.4	2357	367	1400-3560	13	135	56.7	144.0	2217	370	1510-3130
13	132	58.4	148.7	2655	464	1840-4300	14	162	59.6	151.4	2537	442	1670-3890
14	177	60.9	154.8	2929	523	1510-4640	15	192	61.6	156.6	2816	390	2050-4100
15	155	62.9	159.9	3397	595	2000-4750	16	131	62.1	157.8	2918	446	2050-4000
16	67	65.8	167.2	3699	619	2270-4640	17	29	63.0	160.1	3000	-	2210-3780
17	23	67.4	171.4	4078	-	2590-4860		7	64.0	162.6	3178	-	2430-3670

¹ From STEWART and SHEPHERD, *Amer. J. Dis. Child.*, 24, 83, 451 (1922)² Original values increased by 8% as an approximate conversion to BTPS (cf. DENBESTEN et al., *J. Allergy*, 30, 514 (1959))Table 5 Ratios of vital capacity (VC), residual volume (RV), total lung capacity (TLC) and forced expiratory volume (FEV₁) to the cube of the height, and other ratios (volumes in litres, heights in metres)³

Age (years)	VC litres	RV litres	TLC litres	100 RV TLC	FEV ₁ litres	FEV ₁ VC
18-19	0.990	0.240	1.230	19.5	0.812	82.0
20-29	1.025	0.275	1.300	21.0	0.818	80.0
30-34	1.020	0.300	1.300	22.5	0.795	78.0
35-39	1.010	0.310	1.320	23.5	0.778	77.0
40-44	1.000	0.320	1.320	24.3	0.757	75.5
45-49	0.990	0.330	1.320	25.0	0.737	74.5
50-54	0.970	0.350	1.320	26.5	0.713	73.5
55-59	0.950	0.370	1.320	28.0	0.684	72.0
60-64	0.930	0.390	1.320	29.5	0.651	70.0
2.1 ⁴ × 100*	17*	31*	22*	11*	19*	13*
Number	3153	1098	1098	1098	2536	2536

* 1% = Coefficient of variance (see page 159).

³ From CARA and MARTIN, in DENBESTEN et al. (Eds.), *L'exploration fonctionnelle du pneumothorax*, Flammarion, Paris, 1964, page 112

Table 6 Maximum expiratory flow rate (MEFR) in children and adults

Age (years)	Number	Method	MEFR (litres ³ /s)		Reference
			Mean	s	
Children 3-5	30	Pneumotachograph	1.8	0.4	1
Men 9-13	16		5.0	0.8	2
14-19	10		7.1	1.3	2
20-29	20		8.0	0.9	2
32-39	16		7.9	1.1	2
40-49	16		7.6	1.0	2
50-59	17		7.3	1.2	2
60-75	11		6.8	1.2	2
Women 14-19	3	HADORN pneumatometer	5.5	(0.9)	2
20-29	11		5.8	0.7	2
30-39	3		6.0	(0.8)	2
40-49	4		5.1	(0.6)	2
50-59	4		4.6	(0.5)	2
60-64	3		5.0	(0.2)	2
Adults 40	37	'Minimus' pneumatometer	6.85	1.89	3

¹ RIVIERA and SNIDER, *Pediatrics*, 30, 117 (1962)² ZEMDNER, H., *Hals und Atm.*, 27, 245 (1960)³ FARRE and BLANC, *Arch. Med. Biol.*, 87, 2361 (1962)

Table 7 Diffusing capacity of the lungs (D_L) in resting subjects

Method	Number	Age (years)	D_L (ml min ⁻¹ mm Hg ⁻¹)		Reference	Remarks
			Mean	95% range (extreme range in brackets)		
<i>CO methods</i>	'Steady state' method	5	23-45	17	(10.5-28.0)	¹
	'Steady state' method	18	18-41	17.6	(10.5-28.7)	²
		7	26-36	20.6	9.6-31.6	³
	Single-breath method	28	8-72	24.9	(11.0-37.5)	⁴
		20	4-13	17.4*	4.8-30.0	⁵
	Continuous breathing method	3	24-46	35.6	(28.4-41.6)	⁶
		15	24-60	25	(19-31)	⁷
<i>O₂ methods</i>	'Steady state' method	6	28-36	21	(12-36)	⁸
		9	22-28	47	-	⁹
	Single-breath method	5	24-46	33	(23-45)	⁶
* Dependent on body surface area:						
Surface area (m ²)		D_L		Surface area (m ²)		D_L
0.8		12.8		1.4		25.4
1.0		17.0		1.6		29.6
1.2		21.2		1.8		33.8

¹ FILLEY et al., *J. clin. Invest.*, 33, 530 (1954).² BATES et al., *J. Physiol.*, 129, 237 (1955).³ MACKLEM and BECKLAKE, *Amer. Rev. resp. Dis.*, 87, 47 (1963).⁴ OCHLIVIE et al., *J. clin. Invest.*, 36, 1 (1957).⁵ GIAMMONA and DALY, *Amer. J. Dis. Child.*, 110, 144 (1965).⁶ HYDE et al., *J. clin. Invest.*, 45, 1178 (1966).⁷ KRUHOFFER, P., *Acta physiol. scand.*, 32, 106 (1954).⁸ LILIENTHAL et al., *Amer. J. Physiol.*, 147, 199 (1946).⁹ HAAB et al., *Helv. physiol. pharmacol. Acta*, 23, C23 (1965).

Table 8 Respiratory resistances in children and adults

	Number	Age (years)	Resistance (cm H ₂ O s l ⁻¹)		Reference
			Mean	s	
Airway resistance	5	4-6	1.93	0.5	¹
	5	10-13	1.49	0.2	¹
	5	10	2.26	0.73	²
	21	22-57	1.50	0.49	³
	12 men	24-46	0.96	0.27	^{2,4}
	7 women	18-30	1.46	0.47	^{2,4}
Pulmonary tissue resistance	5	10	1.31	0.37	²
	12 men	24-46	0.29	0.12	^{2,4}
	7 women	18-30	0.50	0.15	^{2,4}
Total pulmonary resistance	5	10	3.57	0.98	²
	12 men	24-46	1.25	0.28	^{2,4}
	7 women	18-30	1.96	0.45	^{2,4}
	11	18-47	1.9	0.6	⁵
	21	50-89	2.8	0.8	⁵
	7	26-36	1.7	1.1	⁶
	36	-	2.59	0.68	⁷
Thoracic tissue resistance	36	-	1.37	0.63	⁷
Total respiratory resistance	36	-	3.96	0.65	⁷

¹ GIAMMONA and DALY, *Amer. J. Dis. Child.*, 110, 144 (1965).² BACHOFEN and SCHERRER, *J. clin. Invest.*, 46, 133 (1967).³ DUBOIS et al., *J. clin. Invest.*, 35, 327 (1956).⁴ BACHOFEN, H., *Helv. med. Acta*, 33, 108 (1966).⁵ BACHOFEN, H., *J. clin. Invest.*, 36, 1680 (1957).⁶ FRANK et al., *Amer. Rev. resp. Dis.*, 87, 47 (1963).⁷ MACKLEM and BECKLAKE, *Amer. Rev. resp. Dis.*, 87, 47 (1963).⁸ JAEGER, M., *Schweiz. med. Wschr.*, 92, 67 (1962).Table 9 Compliance of the lungs (C_L) in resting adults and children

Number	Age (years)	C_L (ml cm H ₂ O ⁻¹)		Reference	Remarks
		Mean	s		
11	18-47	150	27	¹	Respiratory frequency 20/min
21	50-89	131	38	¹	
12	39	213	60	²	
7	26-36	189	34	³	
12 men	24-46	260	60	⁴	
7 women	18-30	160	50	^{4,5}	
5	10	83	10.2	⁵	

¹ FRANK et al., *J. clin. Invest.*, 36, 1680 (1957).² HAMM et al., *Z. klin. Med.*, 157, 133 (1962).³ MACKLEM and BECKLAKE, *Amer. Rev. resp. Dis.*, 87, 47 (1963).⁴ BACHOFEN, H., *Helv. med. Acta*, 33, 108 (1966).⁵ BACHOFEN and SCHERRER, *J. clin. Invest.*, 46, 133 (1967).Table 10 Work of breathing per breath per millilitre tidal volume in adults¹

	g cm ml ⁻¹	
	Mean	s
Total inspiratory work	2.40	0.50
Elastic inspiratory work	1.80	0.35
Nonelastic inspiratory plus nonelastic expiratory work	1.40	0.30

¹ HAMM and SCHÜLMERICH, *Klin. Wschr.*, 42, 1108 (1964).

lood pressure in various vessels (mm Hg)¹

	Systolic pressure		Diastolic pressure		Mean pressure		Method
	Mean	Range	Mean	Range	Mean	Range	
Right atrium	—	—	—	—	3.5	2.5–6.0	Right heart catheterization
Left atrium	—	—	—	—	6.6	6–9	Left heart catheterization
Right ventricle	25	17.0–31.5	0	–0.5 to +7.0	—	—	Right heart catheterization
Left ventricle	120	105–150	0	–0.5 to +7.0	—	—	Left heart catheterization
Pulmonary artery ...	20	11–29	9	4–13	—	8–19	Right heart catheterization
Pulmonary arterioles	15	—	5	—	—	5–13	Right heart catheterization
Pulmonary veins ...	4	—	8	—	5	3–8	Left of right heart catheterization
Vena cava	—	—	—	—	—1	–5 to +4	Right heart catheterization

Arterial blood pressure

Various methods of measuring blood pressure have been proposed^{2, 4}, and special techniques have been developed for children².

As well as by the World Health Organization³, comparison with intra-arterial measurements has shown that in persons of normal weight the auscultatory method gives readings variously

in full-term infants¹². In children the arterial blood pressure increases gradually with age. Between 12 and 14 years, however, the diastolic pressure tends to fall^{12, 13}, i.e., in the period when sex differences become well marked. In young persons the arterial blood pressure appears to depend mainly on the degree of maturity^{12, 14}, and abnormally high values in the absence of organic disease point to vasomotor instability. The extent to which the

seems to have little effect on the arterial blood pressure, but during very heavy work the systolic pressure often rises to over 180 mm Hg¹⁵, whereas the diastolic pressure increases only slightly. The arterial blood pressure often rises during emotional stress¹⁶. In early pregnancy it tends to be low but rises towards term¹⁷.

Arterial blood pressure (mm Hg) at various ages

Age	Systolic				Diastolic				Reference
	Men		Women		Men		Women		
	Mean	s	Mean	s	Mean	s	Mean	s	
1 day	70	5							33
3 days	72	6							33
9 days	73	6							33
3 weeks	77	5							33
3 months	86	5							33
6-12 months	89	14.5	93	9.1	60	10.0	62	9.3	34
1 year	96	15.2	95	11.9	66	12.3	65	15.0	34
2 years	99	12.4	92	12.2	64	12.3	60	11.7	34
3 years	100	12.4	100	11.2	67	11.7	64	8.3	34
4 years	99	10.1	99	10.6	65	5.1	66	9.8	34
5 years	92	6.0	92	6.5	62	7.5	62	6.5	34
6 years	94	6.5	94	7.0	64	7.5	64	7.0	34
7 years	97	6.5	97	7.0	65	7.5	66	7.5	34
8 years	100	6.5	100	7.0	67	7.0	68	7.0	34
9 years	101	6.5	101	7.0	68	6.5	69	7.0	34
10 years	103	6.5	103	7.0	69	6.0	70	6.5	34
11 years	104	6.5	104	7.0	70	5.5	71	6.5	34
12 years	106	6.5	106	7.0	71	5.0	72	7.0	34
13 years	108	6.5	108	6.5	72	5.0	73	7.5	34
14 years	110	6.5	110	6.5	73	5.0	74	8.5	34
15 years	112	7.0	112	7.0	75	5.5	76	9.5	34
Age	Systolic				Diastolic				Reference
Age	Men		Women		Men		Women		
	Mean	s	Mean	s	Mean	s	Mean	s	
16 years	118	12.2	116	12.1	73	10.3	72	9.6	34
17 years	121	12.9	116	11.5	74	9.4	72	9.2	34
18 years	120	12.0	116	11.4	74	10.0	72	8.6	34
19 years	122	15.0	115	11.9	75	10.3	71	8.9	34
20-24 years	123	13.8	116	11.8	76	9.9	72	9.7	34
25-29 years	125	12.6	127	11.4	78	9.9	72	9.7	34
30-34 years	126	13.6	120	14.0	79	9.7	74	9.1	34
35-39 years	127	14.2	124	13.9	80	10.4	78	10.0	34
40-44 years	129	15.1	127	17.1	81	9.5	80	10.6	34
45-49 years	130	16.9	131	19.5	82	10.8	82	11.6	34
50-54 years	135	19.2	137	21.3	83	11.3	84	12.4	34
55-59 years	139	18.8	139	21.4	84	11.4	84	11.7	34
60-64 years	142	21.1	144	22.3	85	12.4	85	13.0	34
65-69 years	143	26.0	154	29.0	83	9.9	85	13.8	34
70-74 years	145	25.3	159	25.8	82	15.3	85	15.3	34
75-79 years	146	21.6	158	26.5	82	12.9	83	13.1	34
80-84 years	145	25.6	157	28.0	82	9.9	84	13.1	34
85-89 years	145	24.2	154	27.9	79	14.9	82	17.9	34
90-94 years	145	23.4	150	23.6	78	12.1	79	12.1	34
95-106 years	145	27.5	149	23.5	78	12.7	81	12.5	34

Venous blood pressure

The venous blood pressure rises with increasing distance from the heart, so that the highest pressure is in the peripheral vessels. It varies according to the position of the vein in relation to the right atrium, a result of the varying effect of gravity. The venous pressure is usually measured in the median basilic vein of the right arm at the level of the tricuspid valve. In the newborn the venous pressure depends on the time of tying of the umbilical cord.²⁹

Venous blood pressure (mm Hg)³⁰ (median basilic vein at elbow)

	Mean	Range
Children, 3–5 years	3.4	2.2– 4.6
5–10 years	4.3	2.4– 5.4
Adults, men	7.4	3.7–10.3
women	6.9	4.4– 9.4
Dorsal metacarpal veins	9.6	5.2–12.5
Femoral vein	8.2	7.2– 9.4
Abdominal veins	8.5	5.2–11.8
Long saphenous vein	11.0	8.1–14.0
Dorsal digital veins of foot	12.9	9.1–15.4

Capillary blood pressure (mm Hg) (at base of finger nail, hand at level of heart)

	Mean	Range
Direct measurement ³¹		
arterial limb	32	21–48
venous limb	12	6–18
Indirect (bloodless) measurement ³²		
arterioles	47	–
capillaries	27	–

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Blood volume

In men the normal blood volume amounts to 6–8%, in women 5.5–7%, of the body weight (see page 528), depending on the bodily constitution. Of the total quantity, 65–75% is in the venous system, 15–20% in the arteries and 5–7.5% in the capillary bed¹. Blood volumes given by different authorities should not be compared without careful prior scrutiny of the methods of measurement used. The table on page 555 contains selected blood volume values for children and adults. The literature^{1–3} should be consulted for more comprehensive reviews.

The most accurate method of determining the blood volume (BV) is by separate measurement of the plasma volume (PV) and erythrocyte volume (EV):

$$BV = PV + EV \quad (1)$$

A less accurate method is by calculation from the plasma volume and body haematocrit (Ht):

$$BV = 100 \times \frac{PV}{100 - Ht} \quad (2)$$

or from the erythrocyte volume and body haematocrit:

$$BV = 100 \times \frac{EV}{Ht} \quad (3)$$

The body haematocrit is defined as

$$Ht = 100 \times \frac{EV}{PV + EV} \quad (4)$$

and is calculated from the venous haematocrit (Htv):

$$Ht = Htv \times 0.97 \times 0.91 = Htv \times 0.88 \quad (5)$$

The factor of 0.97 allows for the trapped plasma remaining in the erythrocyte column after centrifuging (micro-haematocrit technique⁴), the factor of 0.91 for the lower erythrocyte content in the blood as a whole than in venous blood.

Various methods are available for determining plasma and erythrocyte volume^{3, 5}. The following indicators are used for plasma volume: Evans blue (T-1824), Coomassie blue⁶, dextran, ⁵¹CrCl₃, ⁵⁹Fe citrate, ¹³¹I-human serum albumin, ¹²⁵I-human serum albumin⁷, alkaline phosphatase⁸; indicators for erythrocyte volume are carbon monoxide and erythrocytes tagged with ³²P, ⁴²K or ⁵¹Cr.

Physiological variations

During the first years of life there are considerable differences between the blood volumes of individual children⁹. Divergences in published values for the blood volume of newborn infants^{9–11} and children^{12–14} are probably due to differences in the method of measurement. In the newborn the time of tying of the umbilical cord has an effect on the blood volume¹¹. Regression equations for the blood volume in children in relation to height, weight and body surface area have been derived¹². Up to puberty the blood volume

rd that the relationship to body weight in adults is very similar to that in children¹⁴.

In adults the blood volume is very closely related to the body

- ¹⁴ MARTIN, W. B., *Amer. J. med. Sci.*, 242, 342 (1961), *STANLEY and*
Amer. J. med. Sci., 245, 556 (1963)
¹⁵ BURTON et al., *Transfusion (Phila.)*, 5, 143 (1965), *New England*
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¹⁶ POSTER et al., *J. Lab. clin. Med.*, 65, 530 (1965)
¹⁷ SUGGON et al., *J. Pediatr.*, 55, 163 (1959).

volume, since compared to whites negroes¹⁴ have lower, erythrocyte higher, blood and plasma volumes.

The blood volume is fairly constant, and intake of fluid by either the oral or intravenous route is followed by its very rapid normalization¹⁴. Bed-rest causes a diminution in the blood volume, mainly

1181
The volume has returned to normal at 3-4 months post partum^{24, 31}.

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Blood, erythrocyte and plasma volumes (per kilogramme body weight or square metre body surface area)

	Number	Whole blood				Erythrocytes				Plasma				Ratio body haematocrit venous haematocrit		Method*
		ml/kg		ml/m ²		ml/kg		ml/m ²		ml/kg		ml/m ²				
		Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	
Newborn, 15-30 minutes	50	76.5	7.81	-	-	35.0	5.60	-	-	41.5	3.98	-	-	-	-	T-1824, Ht
Newborn, 24 hours	61	83.3	6.2	-	-	37.7	6.4	-	-	45.6	4.3	-	-	-	-	T-1824, Ht
Children, 3 months	-	87	-	-	-	33	-	-	-	54	-	-	-	-	-	T-1824, Ht
Children, 6 months	-	86	-	-	-	31	-	-	-	55	-	-	-	-	-	T-1824, Ht
Children, 1 year	-	80	-	-	-	28	-	-	-	52	-	-	-	-	-	T-1824, Ht
Children, 8 years	-	80	-	-	-	29	-	-	-	51	-	-	-	-	-	T-1824, Ht
Children, 10 years	-	75	-	-	-	30	-	-	-	45	-	-	-	-	-	T-1824, Ht
Children, 15 years	-	71	-	-	-	30	-	-	-	41	-	-	-	-	-	T-1824, Ht
Men	-	71	-	-	-	33	-	-	-	38	-	-	-	-	-	T-1824, Ht
Women	-	70	-	-	-	29	-	-	-	41	-	-	-	-	-	T-1824, Ht
Men	30	69.1	-	2566	235	29.0	-	1039	123	41.1	-	1527	156	0.950	0.33	T-1824, ⁵¹ Cr
Women	30	62.3	-	2245	191	21.6	-	782	80	40.5	-	1463	162	0.930	0.51	T-1824, ⁵¹ Cr
Men	8	77.6	-	2857	-	31.7	-	1167	-	41.9	-	1690	-	0.913	0.036	¹¹¹ I-HSA, ⁵¹ Cr
Women	4	78.7	-	2700	-	29.1	-	998	-	49.6	-	1702	-	0.913	0.036	¹¹¹ I-HSA, ⁵¹ Cr
Men	22	77.8	4.6	2873	210	29.9	3.5	1109	111	48.0	4.9	1765	171	-	-	¹¹¹ I-HSA, Ht
Women	12	72.7	13.4	2437	358	24.7	5.1	835	151	47.5	8.7	1586	214	-	-	¹¹¹ I-HSA, Ht
Men, 23-44 years	10	69	-	-	-	27	-	-	-	42	-	-	-	-	-	T-1824, ⁵¹ Cr
Men, 71-84 years	7	70	-	-	-	25	-	-	-	45	-	-	-	-	-	T-1824, ⁵¹ Cr
Women, 23-51 years	10	64	-	-	-	22	-	-	-	42	-	-	-	-	-	T-1824, ⁵¹ Cr
Women, 60-74 years	7	57	-	-	-	20	-	-	-	37	-	-	-	-	-	T-1824, ⁵¹ Cr

* T-1824 = Evans blue, ¹¹¹I-HSA = ¹¹¹I human serum albumin, Ht = haematocrit

¹ LOW et al., *Amer. J. Obst. Gynec.*, 86, 856 (1963)

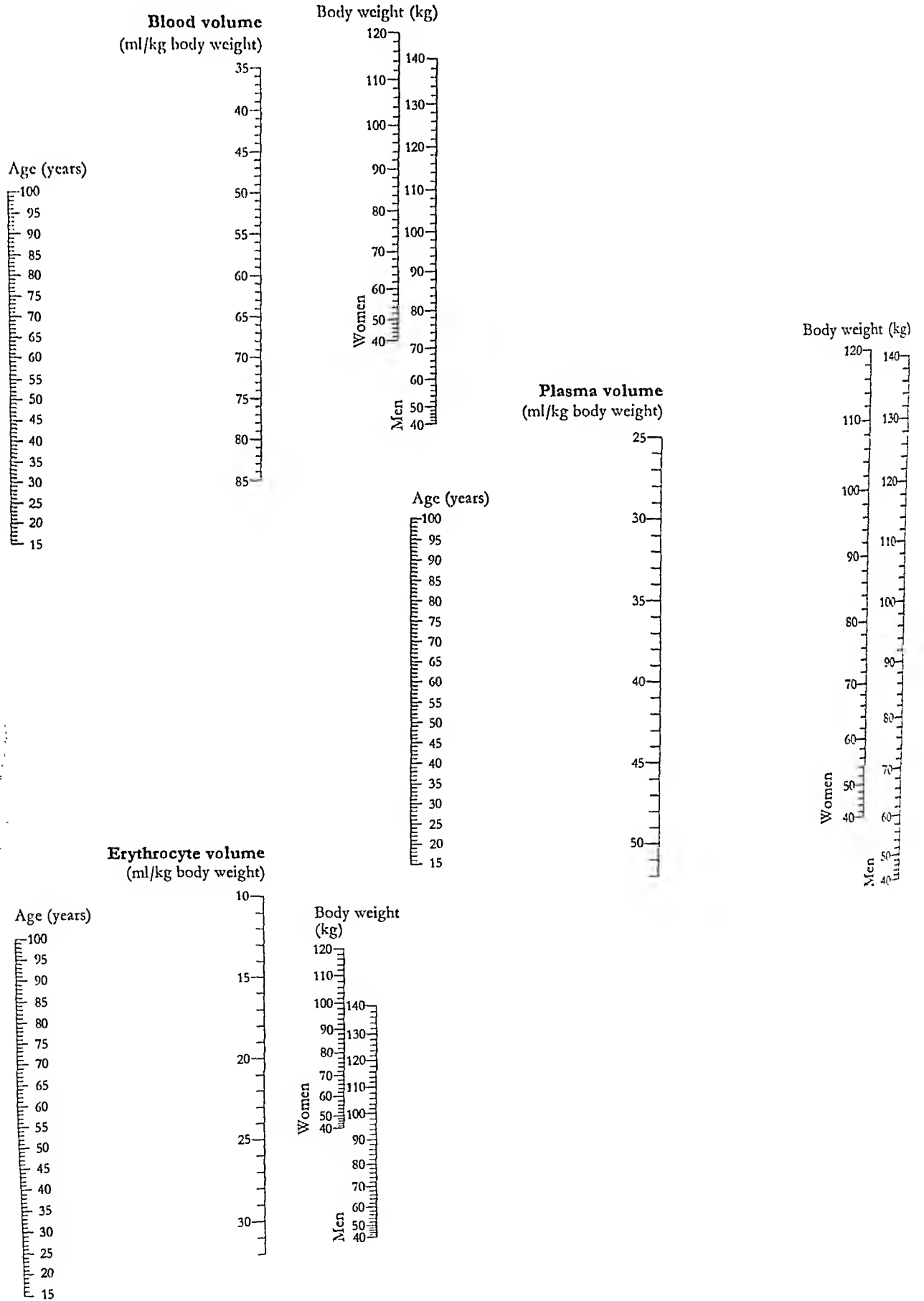
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Nomogram for obtaining blood, plasma and erythrocyte volumes from the age and body weight of adults [DAGHER et al., *Advan Surg.*, 1, 69 (1965)]



	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Colloid-osmotic (oncotic) pressure (at 0 °C)					
Serum (mm Hg)	24.3	(20.6-35.3)	-	¹²	The colloid-osmotic pressure (COP) can be calculated approximately from the albumin and globulin contents by using the formula of KEYS ¹³ (see page 526). Exact calculation requires measurement of the COP of the individual serum protein fractions ¹⁴ . The major part of the COP is accounted for by albumin; fibrinogen has no measurable effect on the COP of the plasma ¹⁵ ; that the COP of the plasma can be equated with that of the serum.
Viscosity					
Relative viscosity (in vitro at 18 °C)					
(a) Whole blood	4.75	(3.80-5.70)	-	¹⁶	Measured on (a, b) 21, (c) 25 fasting subjects with the Hess viscosimeter; (d) in vivo by means of capillaries on subjects with a haematocrit of 40-45%; (e) with the ZEITZSCH capillary viscosimeter. Since blood is a non-Newtonian fluid, viscosity values measured by different methods are not comparable. The dependence of the dynamic viscosity on the shear rate between 10 and 200 s ⁻¹ has been studied by means of a cone-plate viscosimeter ¹⁹ ; for any given haematocrit value the viscosity falls with increasing shear rate. The in vivo viscosity values (d) correspond to a shear rate of ca. 1700 s ⁻¹ . The rheological properties of blood have also been studied in vivo ²⁰ . For determination of viscosity by the falling-ball viscosimeter see KROSCHE and HEIDELMANN ²¹ . The viscosity of whole blood depends mainly on the cell content, i.e., in healthy subjects on the erythrocyte content (see the diagram on page 557) that of plasma on the protein content. The relative viscosity of whole blood is about 0.5 higher in men than in women ^{23, 39} , while in children it is rather lower than in adults ³⁹ . The relative viscosity of venous blood is higher than that of arterial blood ³⁹ . The viscosity of whole blood is pathologically increased in polycythaemia vera ²⁴ , sickle-cell anaemia ²⁵ and leukaemia ²⁶ , that of the serum is increased in hyperglobulinaemia ^{18, 27} , in the presence of a high titre of the rheumatoid factor ¹⁸ , and particularly in macroglobulinaemia ^{18, 27} .
(b) Plasma	2.01	1.67-2.35	0.17	¹⁶	
(c) Serum	1.88	1.58-2.18	0.15	¹⁶	
Dynamic viscosity (centi- poise) (in vivo)					
(d) Whole blood	-	(2.30-2.75)	-	¹⁷	Values depend on the method of measurement (see the table below and text opposite).
Kinematic viscosity (centi- stoke) (in vitro at 37.5 °C)					
(e) Serum	1.15	(1.08-1.22)	-	¹⁸	Calculated from the formula $\frac{1}{2}(a+b/2)$, where a = mm sedimentation in 1 hour, b = mm sedimentation in 2 hours; values from 300 adults. In the method used, a sample of leucocyte-rich plasma is layered on top of cell-free plasma. The LSI is dependent on the properties of the leucocytes but not on those of the plasma; immature leucocyte forms appear to settle out faster. The LSI is increased in acute forms of leukaemia, acute HODGKIN'S disease, tuberculosis and other bacterial infections, and in carcinoma with liver metastases.
Erythrocyte sedimentation rate (sedimentation rate, ESR)	
Leucocyte sedimentation index (LSI) (mm/h)	13.58	3.72-23.4	4.93	²⁰	

Sedimentation rate

Methods	WESTERGREN methods			LINZENMEIER's method ⁷²
	Original ⁷⁰	'Wide tube' modification ⁷¹	WINTROBE's modification ³⁹	
<i>Sedimentation tube</i>				
Blood column	200 mm	100 mm	100 mm	50 mm
Diameter	2.5 mm	5 mm	2.5 mm	5 mm
Anticoagulant	Sodium citrate 3.8% solution	Sodium citrate 3.8% solution	2 parts potassium oxalate + 3 parts am- monium oxalate dry	Sodium citrate 5% solution
Quantity (mg/100 ml mixture)	760	760	200	1000
Resulting dilution of blood	20%	20%	0	20%

Normal values (mornings, fasting)	Sedimentation after							Time for a sedimen- tation of 18 mm (h)	
	1 hour (mm)	2 hours (mm)	24 hours (mm)	1 hour (mm)	2 hours (mm)	1 hour (mm)		Mean ⁷⁵	Range ⁷⁵
	Range	Range	Range	Range	Range	Mean	Range		
Newborn, 1st day	Up to 2 ⁷³	—	—	—	—	—	Up to 2 ⁷³	106	30-185
Newborn, 4th day	—	—	—	—	—	—	—	45	6-120
Newborn, 12th-21st day	—	—	—	—	—	—	—	11	2-40
Males, 12-20 years	—	—	—	—	—	4.7 ⁷⁴	Up to 20 ⁷⁴	—	—
Men.....	3-5	Up to 15	90	2-5	5-14	3.7	Up to 6.5	10	—
Women.....	3-8	Up to 20	100-110	3-8	6-18	9.6	Up to 15	—	3¼-5

Erythrocyte sedimentation rate (ESR)

The mechanism of erythrocyte sedimentation^{29, 30} is only partly understood. Three phases can be distinguished. In the first phase

the rate of sedimentation depends on the extent to which the agglomerate. The cause of the adherence of the cells is reversible adsorption of certain plasma proteins by so-called sedimentation receptors on the cell surface. These receptors probably consist of cerebroside³¹, while the plasma proteins involved can be divided into so-called agglutinins³² and a supplement³³. Except when they are present at very high concentrations, the agglutinins

are present when the sedimentation rate is increased.

A lysophosphatide attaches itself to the serum albumin to form an albumin-lipid complex that inhibits sedimentation of the erythrocytes.

The biological significance of an increase in the sedimentation rate is still obscure. Since a number of substances that inhibit inflammation also inhibit an increase in the sedimentation rate in

Other factors affecting the sedimentation rate are

size, shape (sickle-cell erythrocytes have a lower sedimentation rate than normal erythrocytes), haemoglobin content and number of the erythrocytes.

length of the column of blood (a short column shows a slower

rate)

Physiological variations: The sedimentation rate is more constant in men than in women, this is not due to the menstrual cycle, changes during which are small and of no clinical significance²⁹. In pregnancy, the rate begins to increase at the 3rd to 4th month and does not return to normal until the 3rd or 4th week post partum^{29, 40}. In the newborn the sedimentation rate is greatly reduced (see the table on page 558), in older adults rather high⁴¹.

Pathological variations: The sedimentation rate is reduced in polycythemia, congestive heart failure, diseases of the liver parenchyma,

Guiding principles in practice²⁹

picture, 20-30 hours usually elapse before a change in the sedimentation rate is observed.

2 Daily fluctuations in the sedimentation rate are insignificant. usually it is sufficient to measure the 1- and 2-hour values. In any particular blood sample the measured values vary from method to method. Values show marked differences in any or individual, so that a knowledge of his minimal values when in good health is important.

3 A marked increase in the sedimentation rate is an objective essential,

4 An exceptionally large and rapid increase in the sedimentation rate reaching a maximum in 15-20 minutes points strongly to a plasmacytoma or macroglobulinaemia.

5 A marked and persistent increase in the sedimentation rate that cannot be otherwise accounted for should raise suspicion of carcinoma. In these circumstances the patient should continue to be examined at intervals until the cause of the increase is revealed.

6 A normal sedimentation rate never excludes the possibility of disease, even a severe progressive one such as tuberculosis or

observed in vagotonia

7 In rare cases a marked increase in the sedimentation rate is accompanied by a completely normal plasma protein pattern for instance in decompensated pernicious anaemia. There is no correlation, however, between the sedimentation rate and the fibrinogen, globulin or total protein content of the blood.

9 The sedimentation rate is often less affected by the disease itself than by the secondary complications, such as pneumonia, thrombophlebitis, infarction of the lung, intercurrent infections etc. Anticoagulant therapy often delays normalization of the sedimentation rate for a considerable time. While drugs in general have no direct effect on the sedimentation rate they may have a secondary effect due to damage to the liver parenchyma.

10 Measurement of the sedimentation rate provides an opportunity of examining the plasma for colour and clarity (golden-yellow in haemolysis, unusually clear in iron deficiency, straw-coloured

naked eye

	Mean	95% range (extreme range in brackets)	s	Reference	Remarks
Surface tension (20 °C, dyn cm ⁻¹)					
serum	56.2	-	-	42	Values measured by torsion balance in 82 fasting subjects between 20 and 36 years of age
Refractive index (20 °C)	-	(1.34946-	-	43	

	Mean	95% range (extreme range in brackets)	<i>t</i>	Refer- ence	Remarks	
Specific heat (cal deg ⁻¹ g ⁻¹)						
Whole blood	0.87	—	—	45		
Plasma	0.94	—	—	45		
Erythrocytes	0.77	—	—	45		
Specific conductivity (25 °C, S cm ⁻¹)						
Serum.....	0.01190	(0.01173– 0.01229)	—	46	The specific conductivity and total protein content of the serum can be used to calculate the total cations (see page 562).	
Electrophoretic mobility (anodic) (μm s ⁻¹ V ⁻¹ cm)						
(a) Erythrocytes	1.080	1.064–1.096	0.008	47	Values from (a) 10 subjects (pH 7.2 in phosphate-buffered saline), (b) 28 subjects (citrate blood). The electrophoretic mobility of blood cells is determined mainly by the carboxyl groups of the sialic acid present on the cell surface ⁴⁹ . Each type of cell has a characteristic mobility; that of the erythrocytes is independent of race, sex, age and blood grouping ⁵² . The leucocytes have an increased mobility ^{48, 61} in chronic and acute myelosis, lymphadenosis, Hodgkin's disease and in the presence of tumours with bone metastases. Erythrocytes have a lower mobility in the serum of cancer patients ⁵³ .	
(b) Erythrocytes	1.270	1.236–1.304	0.017	48		
(b) Granulocytes.....	0.840	0.790–0.890	0.025	48		
(b) Lymphocytes	1.060	1.006–1.114	0.027	48		
(b) Thrombocytes	0.120	0.020–0.220	0.050	48		
Surface density of electric charge (esu cm ⁻²)						
Erythrocytes	3500	—	—	50	Calculated from the electrophoretic mobility. Assuming the erythrocyte surface to be 163 μm ² , the electric charge per erythrocyte is 11.9 × 10 ⁶ esu.	
Redox potential (mV)						
Whole venous blood						
(a) To calomel electrode	—	—260 to —300	—	54	The range given embraces 83% of 550 measurements made in vitro by the method of ZIEGLER ⁵⁵ using a weakly polarized platinum electrode. The redox potential of blood is determined by the ratio of dehydroascorbic acid to ascorbic acid.	
(b) To hydrogen electrode ..	—	—12 to —52	—	54		
pH value (38 °C)						
(a) Umbilical artery, whole blood	7.21	(7.05–7.38)	—	56	Values from (a) 19, (b) 12, (c) 13, (d) 15, (e) 29, (f, g, h, k) each 20, (i) 55 and (j) 9 subjects measured by pH electrode; values (d, f, g, h, k) are on the NBS pH scale, values (e, j) on the HITCHCOCK-TAYLOR pH scale. On the theoretical basis of pH measurement see page 278. The clinical measurement of pH has been much discussed ^{60, 65–67} . pH values are comparable on when the nature of the standard buffer used is known; use of the National Bureau of Standards buffer scale is recommended (for the NBS pH scale see page 279). Measurements should be made at 37 °C and not 38 °C ⁶⁴ . Heparin is a suitable anticoagulant, but not oxalate, citrate or EDTA ⁶⁶ . In completely resting subjects there is no difference between the values in plasma and whole blood ⁶⁵ , but during bodily activity the arterial plasma is slightly more alkaline than the arterial whole blood (maximum difference 0.1 pH units at an oxygen saturation of 98%). The pH value of the capillary blood is almost the same as that of the arterial blood ^{59, 60} , the former being on the average 0.008 pH units more alkaline than the latter. In the limbs the venous plasma is up to 0.03 pH units less alkaline than the arterial plasma ⁵⁹ . In the newborn the blood pH is low ^{56, 68} , in pregnant women rather high ⁶⁹ . In acute disturbances of acid-base balance the blood pH may briefly fall to 6.8 or rise to 7.8 ⁶⁰ ; in chronic diseases it usually lies between 7.2 and 7.5. The pH value of the blood is extremely low in diabetic coma and severe renal insufficiency, very high in acute hyperventilation accompanied by anaesthesia and following protracted loss of hydrogen ions, for instance in vomiting.	
(a) Umbilical vein, whole blood	7.32	(7.23–7.42)	—	56		
Arterial whole blood						
(b) Infants, 1–4 weeks	7.377	7.315–7.439	0.031	57		
(c) Infants, 4–16 months	7.432	7.366–7.498	0.033	57		
(d) Adults	7.424	7.386–7.462	0.019	58		
(e) Adults	7.392	—	—	59		
Capillary whole blood						
(f) Men	7.390	7.360–7.420	0.015	60		
(g) Women	7.398	7.366–7.430	0.016	60		
Arterial plasma						
(h) Adults	7.39	7.35–7.43	0.018	61		
Venous plasma						
(i) Adults	7.398	7.378–7.418	0.010	62		
Erythrocytes						
(j) Adults	7.209	7.175–7.243	0.017	63		
(k) Adults	7.19	7.15–7.23	0.022	61		
Capillary whole blood (37 °C)						
(f) Men	7.405	7.375–7.435	—	64		
(g) Women	7.412	7.391–7.435	—	64		

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inorganic substances The references see pages 567-569

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)		Reference	Mean	95% range (extreme range in brackets)		Reference	
Water									
(a) (g/l)	350	735-865	-	1	945	(330-955)	-	1	Values (a) from 128 subjects. The water content of the erythrocytes increases as the haematocrit content falls ¹ . The water content of the plasma is highest in resting sedentary subjects and increases during physical effort. The water content of the leucocytes varies with the type and degree of maturity ² .
(b) (g/l)	713	653-733	19	2					
(c) (g/l)	641.3	634-719	13.6	3					
(d) (g/l)	616	602-624	9.0	127					
Dry substance									
(a) (g/l)	265	-	-	-	80	-	-	-	Values (a) calculated from the water content and specific gravity, (b) measured in 128 subjects. About 90% of the dry substance of whole blood consists of organic substances.
(b) (g/l)	324	316-332	9.0	127					
Total cations									
(a) Arterial blood = Σc_1					152.9	147-157	2.2	4	Values (a) from 44 men by electroanalysis, (b) calculated by addition of the potassium, sodium, magnesium and calcium ions. The total serum cations are increased in premature infants during the
(b) Venous blood = Σc_2					154.1	149-159	2.6	4	
(c) (mEq/kg H ₂ O)	556	540-570	-	3	163	-	-	3	

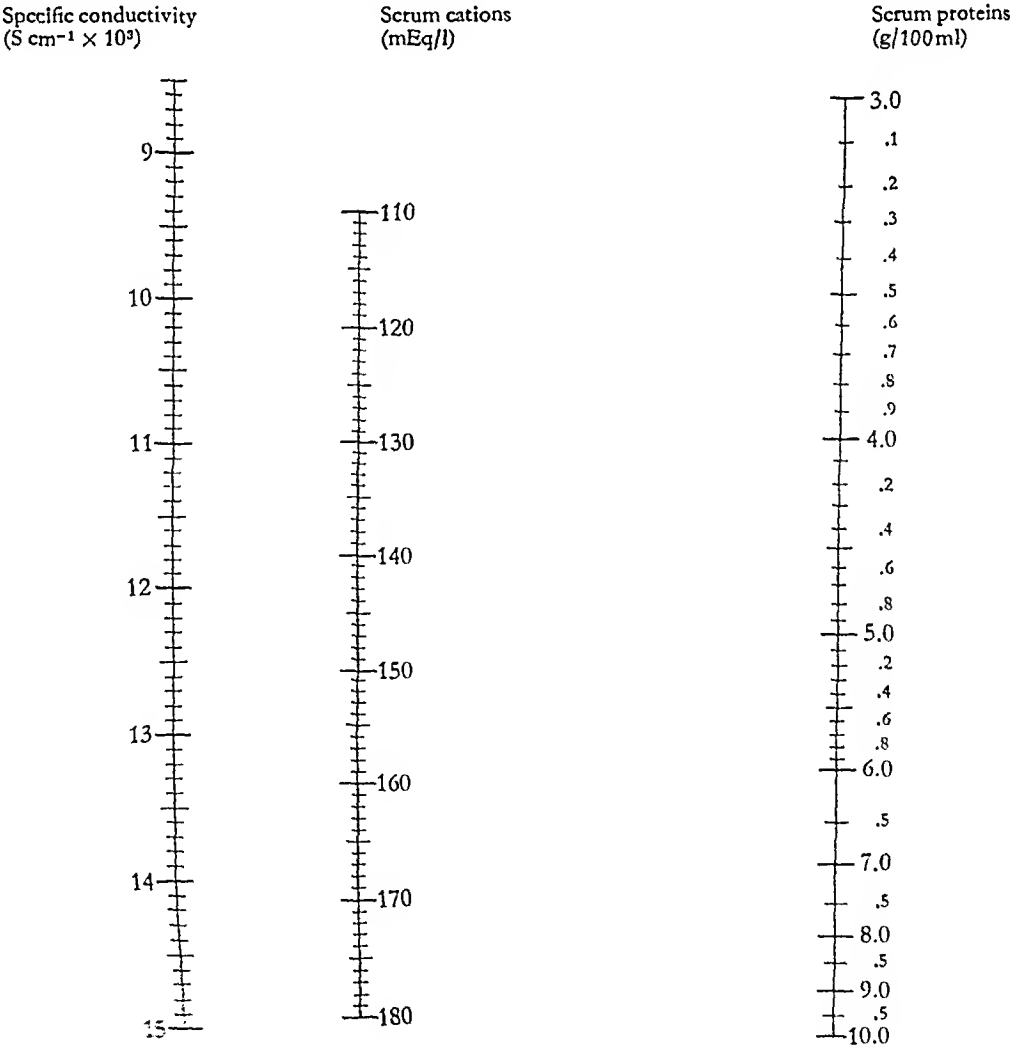
(For references see pages 567–568)

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Bicarbonate (mEq/l).....	11.2	Erythrocytes: 10.9–11.5	0.15	8	24.9	21.3–28.5	1.79	9	Erythrocyte values from 15 subjects. See: 'Blood Gases', page 571.
Chloride (mEq/l)									
(a) Umbilical vein blood	103.3	94.1–113	4.6	10	Values from (a) 14, (b) 20, (c) 157, (f) 37 subjects measured metrically, (b,c) mercurimetrically, (b,c) argentometrically. An autor perometric method of chlorid nation has been described ^{16,17} whole blood comes into con air, CO ₂ passes out of the ery and is replaced by chloride plasma (chloride shift); in de serum chloride the erythrocyt therefore be separated as far a with the exclusion of air.
(a) Newborn, 2 days.....	102.8	88.6–117	7.1	10	
(b) Infants, 3 months.....	113.6	83.2–144	15.2	11	
(c) Adults	–	(77–88)	–	12	102.7	(99–110)	–	12	
(d) Adults	106	101–111	2.5	13	
(e) Adults	–	Erythrocytes: (52–65)	–	14					
(f) Adults	67.9	58.9–76.9	4.5	15					

The chloride content of cord blood is roughly the same as that of the maternal blood¹⁷; that of the serum rather higher in infants than in adults¹⁷. The serum chloride level is pathologically increased after protracted dehydration, in renal hyperchloraemic acidosis (LIGHTWOOD and ALBRIGHT types), in respiratory alkalosis, after head injuries and during treatment with corticosteroids; it is decreased by severe sweating without adequate chloride intake, by

loss of digestive juices (especially gastric juice), by burns, by expansion of extracellular fluid (pneumonia, water intoxication), in injury to tubules, in adrenocortical insufficiency (ADDISON'S disease), during treatment with certain diuretic agents, in respiratory acidosis and occasionally in ketosis accompanied by diuresis.

Nomogram for obtaining the serum cation concentration from the specific conductivity and protein content of the serum LUPKIN and SUNDERMAN, *Techn. Bull. Registry med. Technologists*, 7, 118 [1946], supplement to *Amer. J. clin. Path.*, 16 [1946]



	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	n	Refer- ence	Mean	95% range (extreme range in brackets)	n	Refer- ence	
Phosphorus (mg/l)									
(a) Total phosphorus.....	370	(314-443)	-	10	112	(89-149)	-	10	Values from (a) 42, (b) 464, (c) 121, whole blood; 42, (d, serum) 22, (e) (f) 42, (g, erythrocytes) 20, (g, sera) 42 subjects, values (f) exclude lipid phosphorus.
inorganic phosphorus	719	Erythrocytes (609-867)	-	10					The phosphorus of the erythrocytes consists mainly of phosphoric acid esters (nucleotides, sugar phosphates and glycerol diphosphate), with only small amounts of inorganic phosphate. In serum, lipid phosphorus predominates (see under 'Phosphatides', page 601).
(b) New born, 1 week..	29	(21-38)	-	10	60.3	(37-85)	-	19	<i>Serum inorganic phosphate.</i> Determination should be made in fasting serum. I methods see the literature ²⁴ . The serum phosphate consists of about 80% primary phosphate and about 20% secondary phosphate, depending on the plasma amounts are protein-bound ²⁵ .
(c) Juveniles, 1-19 years...	24	Erythrocytes (9.1-33)	-	10	48	(36-59)	-	20	The serum phosphate level is high during the first days of life ^{17, 18, 26} , is then it is markedly higher than in adults but falls to the adult level when ossification of the skeleton is complete ²⁷ .
(d) Adults ..	2.7	(0.5-4.9)	11	22	33.6	25.6-41.6	40	21	The level begins to increase at about age of 50 ²⁸ . In men and women the levels are about the same ²⁸ except during pregnancy, when there is a marked reduction ²⁹ . On phosphate metabolism see the literature ³⁰ .
(e) Phosphoric ester phosphorus	231	Whole blood (186-286)	-	10	34	(25-45)	-	10	The serum phosphate level is pathologically increased in hypoparathyroidism, pseudohypoparathyroidism, renal insufficiency, vitamin D intoxication, and occasionally in idiopathic hypercalcaemia. It is decreased in hyperparathyroidism, impaired calcium and phosphate absorption, vitamin D-deficient rickets, renal tubular acidosis (Albright type), the FANCONI syndrome and phosphate diabetes.
(f) Lipid phosphorus	497	Erythrocytes (385-587)	-	10					
(g) Lipid phosphorus	137	Erythrocytes 124-150	6.5	23	83	(69-97)	-	10	
Sulphur (mg/l)									
(a) Total sulphur	1221	-	-	21	780	-	-	-	Plasma values (a) calculated from the whole blood and erythrocyte values; values (b) from 16, (c) from 88 young adults.
(b) Protein sulphur	1900	Erythrocytes	-	21					About 93% of the sulphur in blood is contained in the protein. The sulphur ester fraction contains 3 indoxylsulphuric acid (see page 575) and other conjugated sulphuric acids, the neutral sulphur fraction includes amino acids, glutathione, ergothioneine and other compounds.
(c) Nonprotein sulphur	1180	Whole blood	-	21	740	-	-	-	The serum inorganic sulphate level is increased in renal failure ³² .
Inorganic sulphate sulphur	1859	Erythrocytes	-	21					
Sulphuric ester sulphur					33.8	(29.5-37.5)	-	22	
Neutral sulphur					15.7	(10.0-18.5)	-	22	
(d) Inorganic sulphate (mEq/l)					3.9	(2.5-6.5)	-	22	
					14.2	(9.0-19.5)	-	22	
Bromide (mg/l)									
(a) (mg/kg)	3.72	(2.27-5.27)	-	20	2.8	(0.7-13.3)	-	20	Values (a) from 5 subjects determined by neutron activation. The bromide content of the blood appears to fluctuate widely from one individual to another. It is increased by medication with bromine compounds; levels over 2.5 g/l serum are definitely toxic ³⁷ .
Fluoride (mg/l)									
(a)	0.13	(0.04-0.36)	-	20	-	(0.14-0.19)	-	20	Values (a) for whole blood from 37 women; lower values have been recorded in the newborn and their mothers. Serum values from subjects whose drinking
(b)					0.014	-	0.008	120	

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Iodine ($\mu\text{g/l}$)									
(a) Total iodine.....	52.1	(38-60)	-	41	Values from (a) 12, (b) 11, (c) 12, (f) 38, (g) 91, (h) 2 subjects; values determined kaline digestion, (b) ¹³² I trace acid digestion, (c-i) pe digestion. For methods see ^{47, 48} .
(b) Inorganic iodine.....	2.8	(1.0-5.2)	-	42	
Protein-bound iodine									
(c) Cord blood.....	79	(67-92)	-	43	
(n) Adults.....	48.1	(35-56)	-	41	
(d) Adults.....	52	32-72	10	44	
Butanol-extractable iodine									
(e) Newborn, 2-6 days....	-	(70-117)	-	45	
(f) Children, 1 month-10 years.....	55	39-71	8	46	
(g) Juveniles, 11-18 years..	42	30-54	6	46	
(h) Men.....	50.0	33.0-67.0	8.5	46	
(i) Women.....	44.6	31.8-57.4	6.4	46	

The inorganic serum iodine level depends on the iodine intake; with a normal intake the serum iodine is almost exclusively organic. The protein-bound iodine consists of the tetra-, tri- and di-iodothyronines and part of the mono-iodothyronine, while the butanol-extractable iodine comprises only tetra- and

tri-iodothyronine. The serum protein-bound iodine is higher in and during pregnancy^{43, 50}, and also higher in newborn than in old^{43, 45}; it is increased in hyperthyroidism (80-300 $\mu\text{g/l}$) and decreased in hypothyroidism (0-40 $\mu\text{g/l}$)⁴⁷. On iodine metabolism see the literature!

Thiocyanate (mg/l).....	0.80	(0.44-1.14)	-	52	Values from 52 nonsmoker values are found in smokers; patients with hyperplasia of the
Borate (as boron, mg/l)....	0.25	(0.00-1.25)	-	53	Values from 34 children; large due for instance to excessive through the skin from using preparations, are toxic.
Nitrite ($\mu\text{g/l}$).....	8	(0-16)	-	54	
ate (as SiO_2, mg/l)....	8.3	3.5-13.1	2.4	55	Values from 264 subjects; no d due to age, sex or disease (incl. cosis) were found.
Potassium (mEq/l)		Erythrocytes:							
(a) Umbilical vein blood...	99.6	97-102	-	10	7.79	3.79-11.8	2.0	10	Values from (a, erythrocytes) rum 14, (b) 12, (c) 13, (d, eryt 20, (d, serum) 157, (e) 37, (f, 106, (g, serum) 22, (h) 128, (i) jects, all by flame photometry tails of method ⁵⁹ and the thrombocytes on potassium nation in serum see the literat
(a) Newborn, 1 day.....	105	100-108	-	10	6.19	4.73-7.65	0.73	10	
(a) Newborn, 2 days.....	107	100-114	-	10	5.92	4.32-7.52	0.8	10	
(b) Children, 3 months.....	5.24	4.30-6.18	0.47	11	
(c) Children, 18 months....	4.72	3.54-5.90	0.59	11	
(d) Adults.....	81.7	68.3-95.1	6.7	56	4.30	3.40-5.20	0.45	13	
(e) Adults.....	88	76-100	6	15	4.05	3.37-4.73	0.34	15	
(f) Adults.....	3.7	3.1-4.3	0.31	127	
(g) Adults.....	4.4	3.6-5.2	0.39	127	
(h) (mEq/kg).....	89.6	82-97	3.6	127					
		Thrombocytes:							
(i) (mEq/kg).....	89.7	73.9-106	7.9	57					
(k) (mEq/kg).....	69.1	65-71	-	58					

The potassium content of the cord serum is significantly higher than that of the maternal serum¹⁷; in infants it is significantly higher than in adults¹¹. There is no noticeable change in the potassium level in the blood between the ages of 25 and 97⁶¹.

The serum potassium level is pathologically increased by rapid infusion of potassium salts and in massive haemolysis, acute tissue breakdown, adrenocortical insufficiency (Addison's disease, hypoadosteronism), renal failure

accompanied by oliguria or anuria and untreated diabetic ketosis; it is logically decreased by inadequate potassium intake or absorption, by digestive juices (diarrhoea, vomiting), and in adrenocortical hyperthyming (hyperaldosteronism, Cushing's syndrome, corticosteroid therapy disease accompanied by polyuria, medication with diuretic agents, tubular acidosis, FANCONI's syndrome, and diabetic ketosis during treatment.

(For references see pages 567-568)

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
odium (mEq/l)									
Umbilical vein blood	146.8	131-163	8.1	10	Values from (a) 14, (b) 20, (c) 37, (d) 157, (e) 20, (f) 106, (g) 128 subjects by (a-d, f, g) flame photometry, (e) neutron activation. On the flame photometric method ²⁹ and the effect of serum proteins on assay see the literature ^{27, 28} .
Newborn, 1 day	146.4	133-159	6.5	10	
Newborn, 2 days	148.7	140-157	4.3	10	
Adults	16.4	Erythrocytes ^a 10-22	3.0	88	144.5	138-151	3.3	88	
Adults	8.7	5.1-13.1	-	18	143.1	136-151	3.8	18	
Adults	138	132-144	3	13	
Adults	142.6	138-148	2.45	82	
Adults	138.4	132-145	3.07	127	
(mEq/kg) ...	10.9	8.3-13.5	1.3	127					
(mEq/kg) ...	27.0	Thrombocytes 25-28	-	88					

The sodium content of the erythrocytes is rather low during pregnancy¹⁷. The

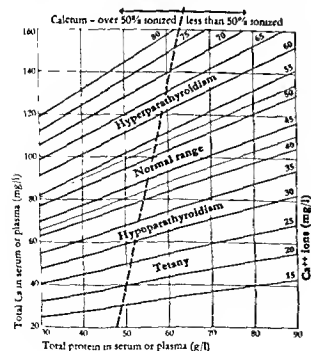
intoxication (for infants particularly a danger), adrenocortical hyperfunction-

The serum sodium level is pathologically increased in dehydration, sodium

excess, and diabetic ketosis

Calcium (mEq/l)

(a) Cord blood	5.5	-	-	88	Values from (a) 3, (b) 48, (d) 70, (e) 21, (f) 35, (g) 50 subjects by (a, d, e, f) EDTA titration, (b) oxalate precipitation, (c, g) flame photometry. The oxalate-precipitation and flame photometric methods give rather higher values than EDTA titration ^{27, 28} . On the flame photometric method see MacIver ^{70, 71} .
(b) Adults	5.09	4.7-5.5	0.22	88	
(c) Adults	5.2	4.8-5.6	0.2	87	
(d) 16-59 years	4.74	4.56-4.92	0.09	128	
(e) 60-70 years	4.60	4.36-4.84	0.12	129	
(f) Adults	4.9	4.6-5.2	0.13	88	
Protein-bound	1.8	1.4-2.2	0.18	88	
Ionized	2.9	2.7-3.1	0.10	88	
Complex	0.1	0-0.3	0.10	88	
(g) (mEq/kg).	0.12	Erythrocytes 0.05-0.19	0.034	2				



The serum calcium is increased in ...

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Magnesium (mEq/l)									
		Erythrocytes:							
(a) Cord blood	4.4	—	—	65	1.64	—	—	65	Values from (a) 3, (b) 77, (c, erythrocytes) 54, (c, serum) 46, (d) 40, (f) 100, (g) 58, (h) 97 subjects by EDTA titration, (c, h) titanium y method, (d) ammonium phosphat precipitation, (e) emission flame p metry, (f, i, k) absorption flame p metry, (g) fluorometrically with droxyquinoline. On the emission photometric method see MACINTY
(b) Adults	5.3	4.24-6.36	0.53	65	2.00	1.70-2.30	0.15	65	
(c) Adults	4.78	3.30-6.26	0.74	76	1.70	1.30-2.10	0.20	76	
(d) Adults	4.93	3.87-5.99	0.53	76	1.73	1.45-2.01	0.14	76	
(e) Adults	1.66	1.50-1.82	0.08	77	
(f) Adults	1.74	1.52-1.96	0.11	78	
(g) Adults	1.89	1.6-2.2	—	79	
(h) Adults	1.80	1.28-2.32	0.26	80	
(i) Before puberty	3.76	(2.86-4.30)	—	83	1.69	(1.50-1.99)	—	83	
(k) After puberty	4.26	(3.68-5.26)	—	83	1.65	(1.36-2.07)	—	83	

For discussion of the discrepancies in the serum magnesium values see the literature⁸¹. The serum magnesium is about 30% protein-bound, 55-60% ionized and 10-15% in the form of complexes^{25, 82}. The serum magnesium level is lower in the newborn and their mothers than in adults⁶⁵. No age or sex differences have been observed in adults⁷⁸. There is an extensive literature on magnesium metabolism^{76, 77, 84, 85}.

The serum magnesium is pathologically increased in kidney disease (the erythro-

cyte magnesium is also increased) and hypothyroidism; it is pathologically decreased in disturbances of magnesium absorption, severe vomiting diarrhoea, hyperparathyroidism, thyrotoxicosis, chronic alcoholism, pri aldosteronism and renal tubular acidosis, and occasionally in liver cirrh. Serum magnesium levels below 1.3 mEq/l are marked by acute convulsio but the peripheral muscle cramps seen in hypocalcaemia do not occur.

Cobalt (µg/l)	0.35	—	—	86	0.29	—	—	87	
Iron (mg/l)									
(a) Cord blood	1.93	—	—	88	Serum values from (a) 21, (b) 17, (c) 161, (d) 33 subjects by (a, b, c) col metry with o-phenanthroline ⁹³ , (c) dipyrldyl method ⁹² . Serum iron also be determined with bathoph anthroline ⁹⁴ .
(b) Children, 3-10 years....	0.86	0.20-1.52	0.33	88	
(c) Boys, 12-19 years	0.946	0.19-1.70	0.376	89	
(d) Girls, 12-19 years	0.917	0.25-1.59	0.335	89	
(e) Men	—	(440-560)	—	90	1.34	0.58-2.10	0.38	88	
(f) Women	—	(420-480)	—	90	—	—	—	—	
(g) Adults	—	0.75-1.75	—	91	
Total iron-binding capacity (= latent or unsaturated iron-binding capacity + serum iron) (mg/l)									
(b) Children, 3-10 years....	4.0	(1.9-4.5)	—	88	
(g) Adults	—	2.5-4.0	—	92	

Most of the iron in the blood is contained in the haemoglobin of the erythrocytes; haemoglobin contains 0.347% iron. The serum iron is in the ferric form and is almost completely contained in the protein transferrin.

Serum iron. There are wide diurnal fluctuations⁹⁵, with values 10-30% higher in the morning than in the evening. In women the values are 10-15% lower than in men⁹² and vary during the menstrual cycle⁹⁶. In pregnant women approaching term the serum iron is 35% lower than in nonpregnant women⁹⁷. In the newborn the level is at first high but falls rapidly during the first 12

hours⁸⁸; it rises again during the first month, falls during the 2nd to 6th month and often remains low up to the age of 2 years before rising to the adult level at school age⁹⁸. On iron metabolism see the literature^{92, 99}.

The serum iron is pathologically increased in haemolytic anaemia, untreated pernicious anaemia, acute hepatitis and idiopathic haemochromatosis, pathologically decreased in iron-deficiency anaemia, infections, the nephrotic syndrome and chronic bleeding.

Copper (mg/l)									
		Erythrocytes:							
(a) Cord blood	1.03	—	—	100	0.51	—	—	88	Erythrocyte values from (a) 3, (d, e) subjects; serum values from (a) 22, (17, (c) 31, (d) 120, (e) 85 subjects. A values determined colorimetrically with dithizone. Copper can also be determined with bathocuproine ⁹⁴ or oval dihydrazide ¹⁰² .
(b) Children, 3-10 years....	1.31	0.77-1.85 (0.99-1.58)	0.27	88	
(c) Men	0.92	0.50-1.34	0.21	88	
(d) Men	0.89	0.72-1.06	0.085	100	1.10	0.79-1.41	0.157	101	
(e) Women	0.89	0.64-1.14	0.127	100	1.20	0.84-1.56	0.178	101	

Some 60% of the erythrocyte copper is contained in the erythrocyte protein, 94% of the serum copper in the caeruloplasmin; both these proteins contain 0.32-0.36% copper. The copper content of the erythrocytes is much more constant than that of the serum, and there is no correlation between the two.

Serum copper. There may be wide fluctuations up to 0.3 mg/l from day to day¹⁰³. During pregnancy the level rises by about 100% and then falls within two weeks post partum to the nonpregnancy level¹⁰⁰. In the newborn it is much lower than in the mother because of the inability of caeruloplasmin to pass the placental barrier. The level rises steeply during the first year and is significantly

higher in children than in adults¹⁰⁴. There is an extensive literature on copper metabolism¹⁰⁵.

The serum copper is pathologically increased in infections, lupus erythematosus, glomerulonephritis, myocardial infarction, haemochromatosis, cirrhosis of various organs, HODGKIN'S disease, acute leukaemia, aplastic anaemia and thyrotoxicosis, as well as during oestrogen therapy; it is pathologically decreased in disturbances of copper absorption, kwashiorkor, hepatolenticular degeneration, idiopathic hypoproteinaemia and loss of caeruloplasmin in the kidneys (in the nephrotic syndrome). In hepatolenticular degeneration the copper not bound to caeruloplasmin is increased.

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	
nganese ($\mu\text{g/l}$)	-	(8.6-16.5)	-	108	-	(1.8-3.1)	-	108	Values (a) by neutron activation, (b) by colorimetry.
.....	~200	Erythrocytes	-	107	~100	-	-	107	
.....	
lybdenum ($\mu\text{g/kg}$) ..	3.3	0-8.3	2.5	38	Values from 5 subjects by neutron activation
ic (mg/l)		Erythrocytes							
Cord blood	3.76	1.56-5.96	1.10	109	1.25	0.59-1.91	0.33	108	Values for whole blood and cells from
Children, 4-11 months	7.77	4.37-11.37	1.70	108	1.27	0.69-1.85	0.29	108	(a) 32, (b) 16, (c) 12, (d) 84, (e) 27, (f) 25 subjects, for serum from (a) 39, (b)
Children, 1-5 years ...	10.55	7.51-13.59	1.52	108	1.30	0.66-1.94	0.32	108	15, (c) 11, (d) 125, (e) 40 subjects; values
Adults	12.44	8.84-16.04	1.80	108	1.09	0.69-1.49	0.20	108	(f, whole blood) determined by neutron activation, all others colorimetrically
.....	5.9	3.7-8.1	1.1	108	1.21	0.83-1.59	0.19	110	About 35% of the serum zinc is bound to proteins. During pregnancy the serum zinc level falls by about 20% ^{108, 111} but that of the erythrocytes and leucocytes remains fairly constant ¹¹² . There is a considerable literature on zinc metabolism ¹¹³ . The serum zinc is pathologically decreased in atrophic cirrhosis of the liver, infections, myocardial infarction and untreated pernicious anaemia. The zinc content of the leucocytes is pathologically decreased in leukosmas ^{109, 112} and cirrhosis of the liver ^{112, 114} .
($\text{mg}/10^{12}$ cells) ..	0.97	Erythrocytes	0.16	109					
($\text{mg}/10^{12}$ cells) ..	14.0	Leucocytes	10.4	108					
		(3.7-43.5)							
luminium ($\mu\text{g/l}$)	140	0-380	120	116	172	156-188	8	118	Serum values from 536 subjects. No dependence on age or sex has been observed
rsenic ($\mu\text{g/l}$)	-	(60-200)	-	117					Values (a) from 8 subjects by neutron activation.
i) ($\mu\text{g/kg}$)	4	0-10	3.1	38					
lead ($\mu\text{g/l}$)									
a)	270	170-370	50	118	29	-	-	118	Values (b) from 100 adults (90% of the values under 100 $\mu\text{g/l}$), values (a) determined spectrographically, (b, c) colorimetrically. Most of the blood lead is in the erythrocytes ¹¹⁵ . Whole-blood values exceeding 400 $\mu\text{g/l}$ indicate an abnormally high lead absorption ¹¹⁶ .
b)	-	(0-200)	-	118					
c)	-	(<300-400)	-	119					
Lithium ($\mu\text{g/l}$)						(3-44)	-	120	
Selenium ($\mu\text{g/kg}$)	120	20-220	50	38					Values from 6 subjects by neutron activation
Other elements									For a detailed list of the elements so far determined in blood see BOWEN ¹²⁷ . Recent assays have been made of barium ^{122, 123} , cadmium ¹²⁴ , chromium ¹²³⁻¹²⁵ , gold ³⁹ , mercury ¹²⁶ , rubidium ¹²² and tin ¹¹⁸ .

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Blood gases (for blood pH values see page 560; for references see page 571)

The normal values given in the table on pages 570 and 571 are for sea level and can be used at altitudes up to 200 m without adjustment. In persons resident at high altitudes the value of P_{CO_2} is reduced as a result of chronic hyperventilation while the pH remains normal owing to complete renal compensation, so that the plasma bicarbonate concentration is also reduced (cf. 'Water and Electrolyte Balance', page 527).

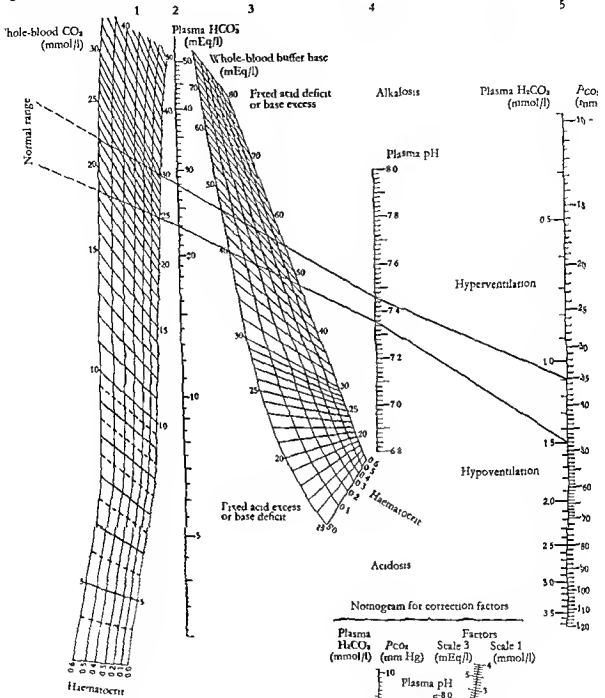
Blood samples for gas analysis must be drawn under anaerobic conditions. Even when they are stored under anaerobic conditions, however, it must be borne in mind that changes due to clotting, glycolysis, autooxidation and sedimentation will occur. Blood from the peripheral subcutaneous veins is not usually suitable for gas analysis. Venous mixed blood is drawn from the pulmonary arteries. Arterial blood should be drawn from the femoral, brachial or radial

arteries. For the micro methods, capillary blood obtained by puncture of the warmed finger tip or of the lobe of the ear is suitable since its gas content is almost identical with that of arterial blood. It has recently been recommended² that blood gas values should be measured at 37 °C instead of 38 °C, or converted to the latter temperature.

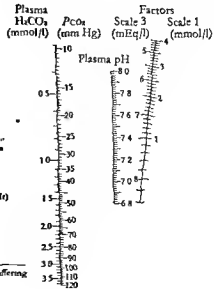
Methods 3-5. Carbon dioxide, oxygen, nitrogen and carbon monoxide are usually determined manometrically by VAN SLIKE'S method or the KOPF-NATELSON micro modification of this method. Carbon dioxide and oxygen can also be measured by mass spectrophotometry, gas chromatography, oxygen capacity and oxygen saturation spectrophotometry, bicarbonate by titration, oxygen pressure by a micrographically, carbon dioxide pressure potentiometrically. Components of the CO_2 -bicarbonate system not measured directly are obtained by calculation using the dissociation equilibrium of carbonic acid (page 527) or by means of nomograms (pages 528 and

Blood Gases

Diagram for the acid-base balance of human blood at 37 °C (from SINGER and HASTINGS, *Medicine [Baltimore]*, 27, 223 [1948])



Nomogram for correction factors



A straight line through points given on axes of the graph - as in example -

$$\text{whole-blood } \text{CO}_2 \text{ corrected} = \text{whole blood } \text{CO}_2 + (f_{\text{factor}} \times U \times Ht)$$

$$\text{whole-blood buffer base corrected} = \text{whole blood buffer base} - (f_{\text{factor}} \times U \times Ht)$$

$$f = \text{haematocrit} = \frac{\text{vol\% of erythrocytes in whole blood}}{100}$$

$$U = 1 - \frac{\text{O}_2 \text{ saturation in \%}}{100}$$

By whole-blood buffer base is understood the base equivalent of the sum of the buffering anions (bicarbonate, haemoglobin, plasma proteinate)

Carbon dioxide content (mmol/l)	Umbilical artery	25	21.4	17.0-25.8	2.2	Amount of CO ₂ extractable by strong acid from blood drawn and sealed under vacuum, 91% as plasma about 3% as haemoglobin, 4% as albumin, 1% as carbinol compounds; in the erythrocytes the corresponding figures are 7%, 87% and 11% (for details see Alastrow ¹⁹)
Umbilical artery	Manometric (van Slyke)	29	19.8	(13.3-25.6)	2.2	
Umbilical vein	Gas chromatographic	25	18.3	13.9-22.7	2.2	
Umbilical vein	Manometric (van Slyke)	32	17.0	(11.1-21.2)	1.1	
Children, 3-11 years, arterial	Gas chromatographic	9	20.4	15.2-22.6	0.6	
Men, arterial	Manometric (van Slyke)	50	21.6	20.4-22.8	0.7	
Men, venous	Manometric (van Slyke)	50	24.6	23.2-26.0	1.83	
Adults, arterial (plasma)	Manometric (van Slyke)	15	26.1	22.4-29.8	0.99	
Men, arterial (plasma)	Manometric (van Slyke)	50	26.6	24.6-28.6	1.43	
Women, arterial (plasma)	Manometric (van Slyke)	50	25.6	22.7-28.5	1.31	
Men, venous (plasma)	Manometric (Korff-Narveson)	7	30.3	27.7-32.9	1.45	
Women, venous (plasma)	Manometric (Korff-Narveson)	8	27.8	24.9-30.7	1.45	
Bicarbonate content (mEq/l)	Adults (plasma)	-	-	21-30	-	
Adults, arterial (plasma)	Calculated	15	24.9	21.3-28.5	1.79	
Adults (erythrocytes)	Calculated	9	11.2	10.9-11.5	0.15	
Standard bicarbonate (mEq/l)	Umbilical vein	-	16.6	11.8-21.4	-	
Children, 1-4 weeks, arterial (plasma)	Calculated	12	21.1	17.8-24.4	1.67	
Children, 4-16 months, arterial (plasma)	Calculated	13	21.0	19.0-23.0	0.99	
Adults, arterial (plasma)	Manometric (van Slyke)	15	25.2	22.4-28.0	1.40	
Men, capillary (plasma)	Calculated	20	-	22.1-25.8	-	
Women, capillary (plasma)	Calculated	20	-	21.3-25.0	-	
Base excess (mEq/l)	Umbilical artery	16	-9.9	-	-	
Umbilical vein	Calculated	16	-6.4	-	-	
Umbilical vein	Calculated	-	-9.5	-16.6 to -2.5	-	
Men, capillary	Calculated	20	-0.1	-2.4 to 2.3	-	
Women, capillary	Calculated	20	-1.0	-3.3 to 1.2	-	
Buffer base (mEq/l)	Umbilical vein	-	37.2	30.8-43.7	-	
Men, arterial	Calculated	153	40.4	46-52	-	
Men, capillary	Calculated	180	50.1	47-53	-	
Women, capillary	Calculated	24	48.0	45-51	-	

[illegible]

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Total nitrogen (g/l).....	34.3	(30.0-41.0)	-	1	13.1	(12.0-14.3)	-	1	Comprises the chemically bound gen. Because of the fibrinogen the nitrogen of the plasma is slightly less than the serum value given here. F KJELDAHL method of N determinis see ARCHIBALD et al. ⁶ . The propo of protein N in the total N is ove in the erythrocytes, over 96% i serum, about 80% in the leucocyte about 90% in the thrombocytes; erythrocytes 94% of the total N i tained in the haemoglobin.
(g/l)	-	Erythrocytes: (57-62)	-	2					
(g/kg).....	55.3	51.7-58.9	1.8	3					
(mg/10 ⁹ cells)	4.61	3.77-5.45	0.42	4					
	10.0	Leucocytes: 0-23.8	6.9	4					
	-	Thrombocytes: (0.31-0.39)	-	5					
Nonprotein nitrogen (NPN) (mg/l)									
(a) Cord blood	311	244-378	33.4	7	Values from (a) 25, (b) 21, (c) 25, (e) 58, (f) 46 subjects by (a-d) me of FOLIN ⁹ , (e, f) method of RAPPAPO. On a high-protein diet the NPN co is increased and the proportion of N is up to 90%; on a low-protein the NPN content is reduced and proportion of urea N is 50% or le. Towards the end of pregnancy the content of the blood decreases and proportion of urea N is small ¹¹ . NPN is pathologically increased in ous kidney diseases, obstruction o urinary tract, burns and shock, and in severe liver damage. See also u 'Urea', below, and page 531.
(b) Newborn, 5-6 days	266	201-331	32.3	7					
(c) Children, 1-6 years	324	253-395	35.7	7					
(d) Adults	331	219-443	56.0	7					
(e) Men	276	202-350	36.9	8	249	177-321	35.9	8	
(f) Women	261	183-339	39.1	8	223	139-307	42.0	8	
		Erythrocytes:							
(e) Men	309	211-407	48.9	8					
(f) Women	318	189-447	64.7	8					
Urea (mg/l)									
(a) Cord blood	294	148-440	73	12	216	158-274	29	7	Values from (a, whole blood) 13 serum) 25, (h) 21, (e) 25, (d) 30, (e) (f) 31, (g) 10 subjects by cleavage urease and determination of NH ₄ NESSLER's reagent ¹⁴ or better BEN LOR's reagent ^{15,16} . In an auton series of assays using diacetylmoime ¹⁷ 90% of the values were be 200 mg/l serum. For calculation of urea content from the NPN see page. The urea content of the blood depe mainly on the protein intake, the am of urine excreted and the functio state of the kidneys. The concentra in the cord blood is determined by i in the maternal blood ¹² ; in preg women it appears to be rather low ⁷ . urea content is increased when pro breakdown in organs is increased i instance in fever and after operatio in disturbances of renal excretion and obstruction of the urinary tract; i decreased frequently in dehydrated tients given N-free solutions ¹⁸ .
(a) Newborn, 3 hours	257	71-443	93	12					
(a) Newborn, 24 hours	318	60-576	129	12					
(b) Newborn, 5-6 days	201	139-263	31	7	
(c) Children, 1-6 years	313	241-385	36	7	
(d) Adults	328	230-426	49	7	
(e) Men	272	156-388	58	8	305	177-433	64	8	
(f) Women	241	131-351	55	8	238	122-354	58	8	
		Erythrocytes:							
(e) Men	232	114-350	59	8					
(f) Women	178	58-298	60	8					
(g) In relation to protein intake									
0.5 } g protein/kg	193	135-251	29	13	
1.5 } body weight/day	386	244-528	71	13	
2.5 }	455	311-599	72	13	
Creatine (mg/l)									
Children, 1-14 weeks	-	(2.2-12.5)	-	19	Serum values by (a) JAFFE reaction, fluorometry with ninhydrin. On i JAFFE reaction see below under 'Cr tinine'. The serum creatine level is son what increased on a diet rich in meat.
Adults									
(a)	27	-	-	20	-	(1.6-4.0)	-	21	
(b)	-	(1.9-7.9)	-	22	
	56.2	Erythrocytes: -	-	23					
Creatinine (mg/l)									
(a) Cord blood	11.8	6.4-17.2	2.7	7	Serum values from (a) 25, (b) 18, (c) 1 (d) 30, (e) 39, (f) 28 subjects; values (e, f) by an automatic method. The JAF reaction often used to determine cr atine and creatinine is not specific a is subject to interference by glucos acetoacetic acid, acetone, ascorbic acid pyruvate, etc. Values also depend o how the sample is prepared; the measured by the enzymatic ²⁵ and ex change ²⁶ methods (true creatinin are about 10-20% less than the JAF reaction values. For further discusio of methods see the literature ^{27,28} .
(b) Children, 4-21 weeks	9.5	7.9-11.1	0.8	7	
(c) Children, 1-6 years	11.9	7.5-16.3	2.2	7	
(d) Adults	6	-	-	20	12.4	6.6-18.2	2.9	7	
(e) Men	8.55	5.3-11.9	1.69	24	
(f) Women	7.12	5.6-8.6	0.77	24	
	4.5	Erythrocytes: -	-	23					

The serum creatinine level is increased by ingestion of creatinine (for instance in roast meat); it is largely proportional to the muscle mass and therefore higher in men than in women (see also page 531). The level is pathologically

increased when endogenous synthesis is increased (as in acromegaly) and when excretion is impaired.

(For references see page 578)

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	n	Reference	Mean	95% range (extreme range in brackets)	n	Reference	
guanidine (mg/l)	-	(<0.4)	-	20	-	-	-	20	Absent from the erythrocytes ²³ .
guanidinoacetic acid (mg/l)	-	(<3)	-	20	-	(2.4-4.4)	-	20	
ethylguanidine (mg/l) ..	-	(<0.2)	-	20	-	-	-	-	
ammonia (mg/l)									
i) Newborn, 0-14 days ..	-	(0.9-1.5)	-	29	Values from (b) whole blood 25, (b, serum) 30, (c) 20, (d) 50, (e) 25 subjects by (a, d, e) diffusion method, (b, c) ion-exchange chromatography. In the newborn the blood ammonia level is higher than in the mother ²⁴ ; it is high in premature infants and newborn with icterus ²⁵ , very often also in patients with incipient hepatic coma ²⁶ .
i) Children	-	(0.07-0.63)	-	29	
j) Adults	0.48	0.22-0.74	0.13	30	0.20	(0.04-0.33)	-	31	
j) Adults, venous blood ..	1.02	0.56-1.48	0.23	33	0.19	0.08-0.30	0.055	32	
k) Adults, arterial blood ..	1.06	0.76-1.36	0.15	33	-	-	-	-	
free amino acids (as α -amino-N) (mg/l)									
a) Cord blood	-	-	-	76.8	36.8-116.8	20	30	30	Values from (a) 25, (b) 32, (c, d) 33 subjects by colorimetric method with ninhydrin. A measure of the amino-acid content is the α -amino-N content, best determined by the gasometric ninhydrin method ²⁷ , though this also measures the α -amino groups of peptides and other substances. In serum the α -amino-N value depends on the manner in which the proteins are precipitated ²⁸ , it is rather higher than in the plasma owing to release of amino acids from the thrombocytes during coagulation (For individual amino acids in blood see page 574.)
b) Children, 6-11 years ..	-	-	-	50.1	24.1-76.1	13	30	30	
c) Men	61	48.4-73.6	6.3	4	42	33.4-50.6	4.3	6	
d) Women	59	48.2-69.8	5.4	4	39	28.0-50.0	5.5	6	
e) Men	87	71.8-102.2	7.6	4	-	-	-	-	
f) Women	90	75.0-105.0	7.5	4	-	-	-	-	
Carnitine (mg/l)					-	(8.6-13.3)	-	49	
Ergothioneine (mg/l)									
(a) Adults	96	Erythrocytes 34-158	31	40	-	-	Values from (a) 94 measurements and (b) 4, (c) 10, (d) 15, (e) 13 subjects. The blood level depends on the ergothioneine content of the diet. Pathological variations have been reported ^{40, 41} .
(b) Cord blood	162	26-256	68	45	-	-	-	-	
(c) Children, 4 days-1 year ..	125	17-233	54	48	-	-	-	-	
(d) Children, 1-12 years ..	200	0-410	105	40	-	-	-	-	
(e) Adults	458	90-826	184	41	-	(<10)	-	41	
Glutathione (mg/l)									
(a) Adults	354	Leucocytes (263-414)	-	43	Values from (a) 10, (b) 102, (c) 10 subjects. Glutathione occurs only in the erythrocytes. In its reduced form it accounts for some 30% of the protein reducing substances of whole blood. There appears to be a close relationship between glutathione stability and the sensitivity of the cells to haemolysis ⁴² .
(b) Newborn, < 48 hours ..	782	Erythrocytes 748-816	16.9	43	-	-	-	-	
(b) Newborn, > 48 hours ..	697	662-732	17.6	43	-	-	-	-	
(c) Adults	-	(586-689)	-	44	-	-	-	-	
(d) Adults	-	-	-	-	-	-	-	-	
(e) Adults	-	-	-	-	-	-	-	-	
Aliphatic amines (as N) (mg/l)	0.30	0.08-0.52	0.11	27	-	Values from 35 subjects. Ethanolamine and dimethylamine predominate.
Ethanolamine (μ mol/kg water)	-	Erythrocytes (<10)	-	41	-	(<10)	-	41	
Phosphoethanolamine (mg/l)	-	Leucocytes (<250)	-	41	-	-	-	-	For plasma values see also the table on page 574.
Cord blood	-	-	2.7	0-5.5	1.4	41	
Maternal blood	-	-	0.5	0-1.1	0.3	41	
(μ mol/kg water)	2651	Leucocytes 451-4851	1100	41	-	-	-	-	

Amino acids

Individual amino acids can be determined by microbiological methods³⁹ or after separation by paper chromatography^{40, 41} or column chromatography^{42, 43}; for a few there are also specific chemical methods. STEIN and MOORE's column-chromatographic separation usually yields 26 amino acids in serum, with a further 6 ninhydrin-positive substances occurring in traces. Normal values are shown in the table below. For further data see the literature (reviews^{43, 44}, values in children^{45, 46}, cord-blood values⁴⁷).

Physiological variations. The amino-acid content of the blood is increased for several hours after a protein-rich meal. It is higher in newborn and particularly premature infants than in older children; in children in general it is rather lower than in adults, though there

are wide individual variations. Values for glutamic acid in children than in adults. In women the amino-acid content of blood shows some dependence on the menstrual cycle: of the luteal phase the alanine, serine, lysine, threonine contents are low, while during pregnancy most amino acids are in rather lower amount than in the luteal phase.

Pathological variations. The serum amino-acid content in liver disease, particularly acute yellow atrophy of the liver, burns and shock, in diabetes with ketosis and in kidney disease (especially β -aminobutyric acid), decreased somewhat. The contents of some amino acids are increased in hereditary disturbances of amino-acid metabolism (see pages 448-450). For further discussion of the pathological variations see the literature.

Free amino acids in the plasma and blood cells of newborn, children and adults (by ion-exchange column chromatography)

	Newborn* 1st day		Adults*		Children** 9 months-2 years		Adults†	Men††		
	Plasma		Plasma		Plasma		Plasma	Plasma ^{‡‡}	Erythrocytes	Leucocytes
	Mean	Range	Mean	Range	Mean	Range	Range	Mean		
	mg/l	mg/l	mg/l	mg/l	$\mu\text{mol/l}$	$\mu\text{mol/l}$	$\mu\text{mol/l}$	$\mu\text{mol/kg}$	$\mu\text{mol/kg}$	$\mu\text{mol/kg}$
Alanine.....	29.4	21.0-36.5	30.7	22.2-44.7	219	99-313	213-472	420	350	6610
β -Alanine.....	1.3	-	0.8	-	0	0	-	-	-	-
α -Aminobutyric acid.....	1.5	0.6-3.0	1.7	1.0-2.4	5	0-17	10-35	-	-	-
β -Aminoisobutyric acid...	-	-	-	-	5	0-22	tracc	-	-	-
Arginine.....	9.4	3.8-15.3	14.3	8.6-26.3	31	11-65	40-140	100	0	330
Asparagine.....	6.0	-	5.7	-	-	-	-	-	-	-
Aspartic acid....	1.1	tracc-2.2	2.2	trace-7.2	2	0-9	1-11	2	370	3500
Citrulline.....	2.8	1.5-5.0	5.3	2.1-9.7	-	-	10-17	-	-	-
Cystine§.....	14.7	8.5-20.2	17.7	11.5-33.7	4	0-40	70-108	110	0	370
Ethanolamine...	3.2	1.6-5.6	0.1	tracc-0.7	-	-	-	-	-	-
Glutamic acid...	7.6	3.0-15.7	8.6	2.5-17.3	-	-	(20-90)	(50)	(320)	(7360)
Glutamine.....	112	79-140	83	61-102	135	46-290	(140-570)	-	-	-
Glycine.....	25.8	16.8-38.6	17.4	10.8-36.6	170	56-308	179-587	220	370	5080
Histidine.....	11.9	7.6-17.7	12.4	9.7-14.5	64	24-112	32-97	80	140	630
Hydroxyproline..	4.2	-	0.92 §§	0.69-1.20 §§	-	-	-	-	-	-
Isoleucine.....	5.2	3.5-6.9	7.1	4.6-11.5	44	26-94	40-99	70	40	2900
Leucine.....	9.5	6.1-14.3	13.2	9.3-17.8	75	45-155	78-176	140	400	6300
Lysine.....	29.3	16.7-39.3	25.4	21.1-30.9	87	45-144	105-207	200	130	2360
Methionine.....	4.4	1.3-6.1	3.2	2.3-3.9	21	3-29	11-30	30	trace	1750
1-Methylhistidine	-	-	-	-	0	0	0-10	-	-	-
3-Methylhistidine	-	-	-	-	0	0	0-8	-	-	-
Ornithine.....	12.1	6.5-20.0	9.2	4.3-16.7	40	10-107	30-64	-	-	-
Phenylalanine...	13.0	6.9-18.2	9.5	6.3-19.2	40	23-69	38-73	50	40	2480
Proline.....	21.3	12.3-31.9	27.1	12.8-51.4	115	51-185	103-290	220	170	2100
Serine.....	17.2	9.9-25.5	11.8	6.8-20.3	92	24-172	76-164	120	150	5100
Taurine.....	17.6	9.3-27.0	8.3	5.7-17.3	49	19-91	32-138	50	36	26000
Threonine.....	25.9	13.6-39.9	19.4	12.2-29.3	60	33-128	76-194	130	160	3400
Tryptophan.....	6.5	trace-13.7	9.8	5.1-14.9	-	-	-	-	-	-
Tyrosine.....	12.6	7.6-18.0	9.1	6.5-11.3	45	11-122	22-83	60	50	1970
Valine.....	16.0	9.4-28.8	19.9	13.6-26.6	127	57-262	168-317	270	330	3750

* Values from 25 infants before the first feed and 8 adults¹²⁹.

** Fasting values from 20 children (VIS, H., quoted by SOUFART, P.⁴³).

† Fasting values from 30 adults assembled from the literature⁴³.

†† Blood-cell values from one man⁴³.

§ Values in μmol are for cystine $\frac{1}{2}$ + cysteine. The plasma of adults contains about 10 mg cystine and about 4 mg cysteine per litre¹³⁰.

§§ Fasting values from 10 men¹³¹.

(For references see page 578)

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
histamine (mg/l).....	2.9	—	—	28					
serumine (mg/l)	1.34	1.14-1.54	0.10	29	Values from 30 subjects. Both amines are found only in the cells
sermidine (mg/l)	0.96	0.86-1.06	0.05	29	
erythocholine (μg/l).....	12.8	0-36.8 (3.2-48.0)	12.0	29	Values from 14 subjects. Higher in asthmatic patients.
choline (mg/l)									
serum choline				—	(244-542)	—	31	The serum choline is almost all in the form of phospholipids.
serum choline	4.4	(2.5-9.9)	—	32	
serum choline	See pages 731 and 733.
serum histamine (μg/l).....	—	(16-89)	—	23	2.6	(0-15)	—	23	Histamine occurs mainly in the leuco- cytes ²⁴ (values in μg per 10 ⁶ cells): neutrophils 3.3, basophils 1680, eosino- phils 160, lymphocytes 0.6, monocytes 1.2, thrombocytes 0.009. The blood histamine is increased in the carcinoid syndrome ²⁵ and particularly in chronic myeloid leukaemia owing to the in- creased number of basophils ²⁶ .
serum histamine (μg/l)	—	(0-27)	—	26					
serum tryptamine	Tryptamine has been found in the blood of a patient with a carcinoid tumour ²⁷ .
serum N-Dimethyltryptamine (μg/l)	39	27-51	6	29			Values from 50 subjects.
serum serotonin (μg/l).	—	(90-180)	—	29	13	1-25	6	29	Most of the blood serotonin is adsorbed on the thrombocytes. It is increased in the carcinoid syndrome ²⁸ , with throm- bocyte values up to 18.5 μg/10 ⁶ cells ²⁹ .
serum serotonin (μg/10 ⁶ cells)	0.336 0.45	Thrombocytes 0.148-0.524 0.13-0.77	0.094 0.16	29 21					
serum indoxylsulphuric acid (indican) (mg/l)									
Men					3	1.2-4.8	0.9	23	Values from (a) 56, (b) 44 subjects. The serum indican is increased in the ne- phrotic syndrome ³⁰ .
Women					3	0.6-5.4	1.2	22	
Sulphatocystositol (mg/l)					—	(0-1)	—	28	
serum indolyl-3-acetic acid (mg/l)					—	(1-2)	—	28	
serum indolyl-3-lactic acid (mg/l)					—	(0.1-1)	—	28	
serum porphyrins									
serum aminolaevulinic acid (mg/l)	—	Erythrocytes ³⁴ (0.25-0.45)	—	29	0.19	0.11-0.27	0.04	22	Serum values from 50 men. Ammo- nium is also formed in the erythro- cytes during the biosynthesis of δ- aminolaevulinic acid ³⁵ .
serum urobilinogen (mg/l)	—	Erythrocytes ³⁴ (0.15-0.40)	—	29					
serum coproporphyrin (μg/l)		Erythrocytes ³⁴							
a) Cord blood	29	0-60 (11-72)	16	29	15	1-29 (7-32)	7	21	Erythrocyte values from (a) 20, (b) 10, (c, d) 20 subjects, serum values from (a) 15, (c, d) 11 subjects. The coproporphyrin content of the erythrocytes shows good correlation with the urobilinogen content ³⁶ . It is often markedly increased in congenital eryth- ropoietic protoporphyria, erythropoietic protoporphyria, erythropoietic protoporphyria, and uroporphyrinogen decarboxylase defi- ciency. It is also increased in liver disease, and is increased in some cases of acute hepatitis. It is also increased in some cases of chronic liver disease.
b) New born, 9-15 days	8	—	—	29					
c) Men	13	5-21 (7-23)	4	29					
d) Women	12	0-26 (3-23)	7	29					

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Protoporphyrin (µg/l)									
(a) Cord blood	540	Erythrocytes: 40-1040 (320-1350)	250	79	Values from (a) 20, (b) 10, (c) 20 subjects. Protoporphyrin absent from the serum ⁶³ . The phyrin content of the erythrocyte count as the coproporphyrin content ⁶⁰ . It is markedly increased in protoporphyrin ⁶¹ deficiency anaemia, slightly in haemolytic anaemia, shows values in lead poisoning, and within the normal limits in anaemia ⁶⁰ .
(b) Newborn, 9-15 days ...	510	-	-	79					
(c) Children, 1-2 years.....	320	-	-	79					
(d) Men	300	150-450 (160-520)	75	79					
(c) Women	370	170-570 (180-510)	100	79					
Uroporphyrin (µg/l).....	-	Erythrocytes: (0-20)	-	76					
Haemoglobin									
Cord blood (mg/l)	80	-	-	84	Values (a) from blood drawn puncture of the heel, (b) from subjects by the benzidine reaction. Haemoglobin is increased in bodily activity and may reach the normal value in highly-trained athletes. The serum haemoglobin is converted to haptoglobin; the maximum capacity is 1.4 g/l serum ⁶⁷ , from 200 subjects. See also 1 and 613.
(a) Newborn (mg/l)	-	(1000-1310)	-	84	
(b) Adults (mg/l)	3.1	(1.6-5.8)	-	85	
(c) Adults (g/l)	158.5	134-173	-	86					
(c) Adults (g/l)	328	Erythrocytes: 299-357	-	86					
Haemiglobin (methaemoglobin) (as % of the haemoglobin)	0.4	(0.0-1.1)	-	88	For spectrophotometric detection see HAINLINE <i>et al.</i> ⁹⁰ . Clinical cyanosis appear at 20% or concentrations of haemiglobin there is danger to life at 70% toxic and congenital haemiglobin (methaemoglobinemia) see J HELLER ⁹² .
	0.65	0.25-1.05	0.20	89					
Carboxyhaemoglobin (as % of the haemoglobin)									
(a) Newborn	0.42	0-1.54 (0.1-1.8)	0.56	93	Values (a) from 20 infants up to 10 years old (infants with Rh and AB incompatibilities had values from 1.9-9.3%), (b) measured in a CO-sphere, (c) measured in a normosphere. Values of 12% and more have been measured in car drivers. Symptoms appear at 15-25%, and life at 65% ⁹¹ .
(b) Adults	0.55	-	-	94					
(c) Adults	3.4	0-8.2	2.4	95					
Verdoglobin (mg/l).....	4	-	-	96					
Bilirubin (mg/l)									
Direct-reacting									
(a) Adults	1.0	(0.5-2.4)	-	97	Values from (a, b) 110, (c) 49, (d) 11, (e) 10, (f) 11, (g) 6, (h) 1 subjects. Determination by BERGH reaction; for modified MALLOY and EVELYN (denatured methanol) see MACDONALD <i>et al.</i> that of JENDRASSIK and GROF (reaction with acetate, benzoate and see GAMBINO <i>et al.</i> ¹⁰² . In the direct spectrophotometric method been used ¹⁰³ . On methods for see the literature ¹⁰⁴ ; purified bilirubin standard is all-important. The direct-reacting bilirubin of reaction represents roughly 1/3 conjugated bilirubin (bilirubin diglucuronide, smaller amounts of bilirubin glucuronide and sulphate), the difference between the total bilirubin and reacting bilirubin (indirect bilirubin) is the free bilirubin. It is uncertain whether direct-reacting bilirubin is present in the serum of healthy persons.
Total									
(b) Adults	6.0	(2.6-14)	-	97	
(c) Premature infants, cord blood	18.5	2.9-34.1	7.8	98	
(d) Newborn, cord blood	15.1	1.7-28.5	6.7	98	
(e) Newborn, 1 day	26.8	0-60.0	16.6	99	
(f) Newborn, 3 days	58.5	2.5-114.5	28.0	99	
(g) Newborn, 5 days	60.6	1.0-120.2	29.8	99	
(h) Newborn, 7 days	50.0	1.4-98.6	24.3	99	
Free									
(i) Men	4.0	1.5-10.5	-	100	
(j) Women	2.8	1.1-7.0	-	100	

The free (unconjugated) bilirubin is normally bound to albumin, the binding capacity of which can be determined¹⁰⁶. The bilirubin of pathological sera can be separated chromatographically into 4 fractions¹⁰⁷, namely free, mono-conjugated, diconjugated and albumin-bound. On the physiology and pathol-

ogy of bilirubin metabolism see the literature^{108, 109}, also pages 363-364 on the opposite page.

Simple jaundice of infants. Owing to deficiency of UDP glucuronyl transferase the liver is incapable of conjugating all the bilirubin present, so that the

disturbances of bilirubin metabolism

Type of jaundice	Nature of metabolic disturbance	Site	Free bilirubin in serum (↑ increased)	Conjugated bilirubin in serum (↑ increased)
		Reticular system	↑	(↑)
			↑↑	(↑)

	passes into the duodenum			
hepatitis, cirrhosis	At several stages of bilirubin metabolism		↑	↑↑

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Reference	Mean	95% range (extreme range in brackets)	s	Reference	
<i>ribose, nucleotides</i>									
lantholn (mg/l)					-	(3-6)	-	113	
ric acid (mg/l)									
Newborn, up to 4 days					55	-	-	114	Serum values from (a) 70, (b) 224, (c) 874, (d) 899 subjects by uricase method; whole blood values from (c) 13, (d) subjects by chromatography, age range of subjects (e, d) 4-88 years. For discussion of methods of uric acid determination see the literature ¹¹⁸ .
Children, 4-9 years					37.3	-	-	113	
Males	23.6	16.0-31.2	3.8	118	48.6	20.8-76.4	13.9	119	
Females	22.7	13.7-31.7	4.5	118	41.8	18.2-65.4	11.8	119	
	25	Lymphocytes	-	117					

The serum uric acid level is pathologically *increased* in gout, in renal injury, and when nucleic acid metabolism is increased (as for instance in myeloid leukaemia and polycythaemia), *decreased* in Wilson's disease and the Fanconi syndrome and by the administration of diuretic drugs.

anthine and hypoxanthine (mg/l)					-	(~1-2)	-	121	
nucleotides (μmol/l)									
adenosine monophosphate	-	(2-14)	-	116					Values from 13 men and 8 women after chromatographic separation. Nucleotides are found only in the cells, and the plasma contains traces at most. Various nucleotides have been determined in whole blood and erythrocytes ¹²⁴ , leucocytes ¹²⁵ and thrombocytes ¹²⁶ . A hereditary type of increased erythrocyte ATP content has been reported ¹²⁷ .
adenosine diphosphate	-	(32-73)	-	116					
adenosine triphosphate	-	(237-586)	-	116					
guanosine triphosphate	-	(13-36)	-	116					
cytosine triphosphate	3	-	-	122					
uridine diphosphate	4.5	-	-	122					
isotauramide-adenine dinucleotide	-	(22-40)	-	116					
As NAD	33.0	-	-	122					
As NADH ₂	4.6	-	-	122					
isotauramide-adenine dinucleotide phosphate	-	(2-15)	-	116					
As NADP	11.6	-	-	122					
As NADPH ₂	16.0	-	-	122					

Blood - Nitrogenous Substances

(For references see page 578)

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Protoporphyrin ($\mu\text{g/l}$)									
(a) Cord blood	540	Erythrocytes: 40-1040 (320-1350)	250	79	Values from (a) 20, (b) 10, (c) 8, (d, e) 20 subjects. Protoporphyrin is almost absent from the serum ⁸³ . The protoporphyrin content of the erythrocytes is not so closely correlated with the reticulocyte count as the coproporphyrin content ⁸⁰ . It is markedly increased in erythropoietic protoporphyria ⁸¹ and iron-deficiency anaemia, slightly increased in haemolytic anaemia, shows very high values in lead poisoning, and remains within the normal limits in pernicious anaemia ⁸⁰ .
(b) Newborn, 9-15 days ...	510	-	-	79					
(c) Children, 1-2 years.....	320	-	-	79					
(d) Men	300	150-450 (160-520)	75	79					
(e) Women	370	170-570 (180-510)	100	79					
Uroporphyrin ($\mu\text{g/l}$).....	-	Erythrocytes: (0-20)	-	76					
Haemoglobin									
Cord blood (mg/l)	80	-	-	84	Values (a) from blood drawn by careful puncture of the heel, (b) from 25 subjects by the benzidine reaction. The serum haemoglobin is increased during bodily activity and may reach 30 times the normal value in highly-trained athletes. The serum haemoglobin is bound to haptoglobin; the maximum binding capacity is 1.4 g/l serum ⁸⁷ . Values (c) from 200 subjects. See also pages 611 and 613.
(a) Newborn (mg/l)	-	(1000-1310)	-	84	
(b) Adults (mg/l)	3.1	(1.6-5.8)	-	85	
(c) Adults (g/l)	158.5	134-173	-	86					
(c) Adults (g/l)	328	Erythrocytes: 299-357	-	86					
Haemiglobin (methaemoglobin) (as % of the haemoglobin)	0.4	(0.0-1.1)	-	88	For spectrophotometric determination see HAINLINE <i>et al.</i> ⁹⁰ . Clinical symptoms (cyanosis) appear at 20% and higher concentrations of haemiglobin ⁹¹ , and there is danger to life at 70% ⁹² . On toxic and congenital haemoglobinaemia (methaemoglobinaemia) see JAFFÉ and HELLER ⁹² .
	0.65	0.25-1.05	0.20	89					
Carboxyhaemoglobin (as % of the haemoglobin)									
(a) Newborn	0.42	0-1.54 (0.1-1.8)	0.56	93	Values (a) from 20 infants up to 4 days old (infants with Rh and ABO incompatibilities had values from 1.9 to 11.9% ⁹³), (b) measured in a CO-free atmosphere, (c) measured in a normal atmosphere. Values of 12% and more have been measured in car drivers. Clinical symptoms appear at 15-25%, danger to life at 65% ⁹¹ .
(b) Adults	0.55	-	-	94					
(c) Adults	3.4	0-8.2	2.4	95					
Verdoglobin (mg/l).....	4	-	-	96					
Bilirubin (mg/l)									
Direct-reacting									
(a) Adults	1.0	(0.5-2.4)	-	97	Values from (a, b) 110, (c) 49, (d) 150, (e) 11, (f) 10, (g) 11, (h) 6, (i) 61, (j) 53 subjects. Determination by VAN DEN BERGH reaction; for modification of MALLORY and EVELYN (denaturing with methanol) see MACDONALD <i>et al.</i> ¹⁰¹ , for that of JENDRASSIK and GROF (acceleration with acetate, benzoate and caffeine) see GAMBINO <i>et al.</i> ¹⁰² . In the newborn a direct spectrophotometric method has been used ^{15,103} . On methods in general see the literature ^{15,104} ; purity of the bilirubin standard is all-important ^{15,105} . The direct-reacting bilirubin of the diazo reaction represents roughly the conjugated bilirubin (bilirubin diglucuronide, smaller amounts of bilirubin monoglucuronide and sulphate), the difference between the total bilirubin and direct-reacting bilirubin (indirect bilirubin) the free bilirubin. It is uncertain whether direct-reacting bilirubin is present in the serum of healthy persons.
Total									
(b) Adults	6.0	(2.6-14)	-	97	
(c) Premature infants, cord blood	18.5	2.9-34.1	7.8	98	
(d) Newborn, cord blood	15.1	1.7-28.5	6.7	98	
(e) Newborn, 1 day	26.8	0-60.0	16.6	99	
(f) Newborn, 3 days	58.5	2.5-114.5	28.0	99	
(g) Newborn, 5 days	60.6	1.0-120.2	29.8	99	
(h) Newborn, 7 days	50.0	1.4-98.6	24.3	99	
Free									
(i) Men	4.0	1.5-10.5	-	100	
(j) Women	2.8	1.1-7.0	-	100	

The free (unconjugated) bilirubin is normally bound to albumin, the binding capacity of which can be determined¹⁰⁶. The bilirubin of pathological sera can be separated chromatographically into 4 fractions¹⁰⁷, namely free, monoconjugated, diconjugated and albumin-bound. On the physiology and pathol-

ogy of bilirubin metabolism see the literature^{108,109}, also pages 363-364 and the table on the opposite page.

Simple jaundice of infants. Owing to deficiency of UDP glucuronyl transferase the liver is incapable of conjugating all the bilirubin present, so that the serum

rubin increases. About 40% of newborn infants have a serum bilirubin level of over 40 mg/dl during the first week.¹⁷⁰ The bilirubin level in the umbilical arterial serum is higher than in the umbilical venous serum.¹⁷¹ The bilirubin level in the newborn. With increasing haemoglobin breakdown the bilirubin level rises, as soon as the binding capacity of the albumin is exceeded.

exceeded, kernicterus may develop. Exchange transfusions are recommended when the serum bilirubin exceeds 193-250 mg/l, depending on the age and health of the child. For further discussion of haemolytic jaundice and kernicterus see the literature.^{58-60, 112}

Aspects of bilirubin metabolism

Type of jaundice	Nature of metabolic disturbance	Site	Free bilirubin in serum (\uparrow increased)	Conjugated bilirubin in serum (\uparrow increased)
Obstructive jaundice		Reticular system	\uparrow $\uparrow\uparrow$	(\downarrow) (\downarrow) —
Haemolytic jaundice (Kern's syndrome) Chronic hyperbilirubinaemia	Impaired transport of free bilirubin	Liver (lysosomes)	\uparrow \uparrow	— —
Jaundice of infants (Gilchrist's jaundice) Neonatal jaundice	Incomplete conjugation of free bilirubin	Liver (microsomes)	\uparrow $\uparrow\uparrow$	— —
Neonatal jaundice (Kern's syndrome) Neonatal jaundice	Impaired excretion of bilirubin glucuronides	Bile capillaries	(\downarrow) (\downarrow) \uparrow	\uparrow \uparrow \uparrow
Neonatal jaundice	Impaired transport of bilirubin glucuronides into the duodenum	Bile ducts	(\downarrow)	$\uparrow\uparrow$
Cholestasis	At several stages of bilirubin metabolism		\uparrow	$\uparrow\uparrow$

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
leucocytes /mm ³									
mg/dl					-	(3-6)	-	112	
mg/dl in, up to 4 days n, 4-9 years					55	-	-	116	Serum values from (a) 70, (b) 224, (c) 874, (d) 899 subjects by uricase method whole-blood values from (c) 13, (d) 15 subjects by chromatography, age range of subjects (c, d) 4-88 years For discussion of methods of uric acid determination see the literature 116.
	23.6	16.0-31.2	3.8	116	37.3	-	-	116	
	22.7	13.7-31.7	4.5	116	43.6	20.8-76.4	13.9	115	
		Erythrocytes	-	117	41.8	18.2-65.4	11.8	115	
	25	-	-						

uric acid level is high in the newborn, in children rather lower than men it remains fairly constant throughout life, in women it is the menopause that in men, higher after it. The upper limit of uric acid method) is 75 mg/l serum in men, 60 mg/l serum in women.¹⁹ There is an extensive literature on uric acid metabolism.²⁰

The serum uric acid level is pathologically increased in gout, in renal injury, and when nucleic acid metabolism is increased (as for instance in myeloid leukaemia and polycythaemia), decreased in Wilson's disease and the Fanconi syndrome and by the administration of uricosuric drugs.

and hypo- e (mg/l)			-	(~1-2)	-	127
les (μmol/l)						
monophosphate	-	(2-14)	-	116		
diphosphate	-	(32-73)	-	126		
triphosphate	-	(287-586)	-	116		
triphosphate	-	(13-36)	-	126		
phosphate	3	-	-	127		
phosphate	4.5	-	-	127		
ude-adenine otide	-	(22-40)	-	116		
D	33.0	-	-	122		
DH ₂	4.6	-	-	122		
ude-adenine otide phosphate	-	(2-15)	-	116		

Values from 13 men and 8 women after chromatographic separation. Nucleotides are found only in the cells, and the plasma contains traces at most. Various nucleotides have been determined in whole blood and erythrocytes¹²⁴, leucocytes¹²⁵ and thrombocytes¹²⁶. A hereditary type of increased erythrocyte ATP content has been reported¹²⁷.

	Whole blood				Plasma or serum				Remarks
	Mean	95% range	s	Reference	Mean	95% range	s	Reference	
Nucleic acids (mg/10 ⁹ cells)									
Ribonucleic acid	8.19	0.91-15.47	3.64	128					
Deoxyribonucleic acid	6.86	4.52-9.20	1.17	128					

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	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	σ	Refer- ence	Mean	95% range (extreme range in brackets)	σ	Refer- ence	
Total proteins (g/l)	-	180-210	-	1	-	Serum 65-80	-	1	In whole blood the haemoglobin of the erythrocytes predominates. It makes up about 94% of the erythrocyte protein, the remainder consisting of anaemia albumin, free globin and various enzymes. For data on the haemoglobin content see page 617. The proteins of the erythrocytes ⁴ and leucocytes ⁵ can be separated by electrophoresis. On the plasma proteins see below and pages 580-583.
	-	Erythrocytes 330-390	-	1					
(mg/10 ⁶ cells)	100	Leucocytes	-	2					
	-	Thrombocytes (1.6-1.8)	-	3					
Fibrinogen (g/l)		2.95	Plasma 2.6-3.3 (2.0-4.0)	0.17	1	Values from 20 subjects. Occurs also in the thrombocytes ⁶ .

Plasma proteins⁷

method), ultracentrifuging, chromatography on ion-exchangers, gel filtration or various methods of electrophoresis (method of Tiselius or using filter paper, starch gel, agar gel, cellulose acetate foil, etc., as carrier). Individual proteins can be identified by im-

the albumin content falls while the β -globulin content rises¹⁵ (see page 582). Differences in the plasma protein level between whites and negroes have often been observed¹⁶.

Several of the serum proteins exhibit allotypy (see under 'Serum Groups', page 634).

References

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Physicochemical and biological characteristics of defined plasma proteins[†]
(For lipoproteins see page 602, for glycoproteins see page 606)

	Grammes per 100 g plasma proteins (%)	Iso- electric point (pH)	Electro- phoretic mobility* (10^{-5} cm ² V ⁻¹ s ⁻¹)	Sedimenta- tion constant S_{20w} (10^{-13} cm ² s ⁻¹ dyn ⁻¹)	Diffusion constant D_{20w} (10^{-7} cm ² s ⁻¹)	Approximate molecular weight	Fun
Prealbumin (tryptophan-rich)	0.1-0.5	—	9.0	4.2	—	61 000	Thyro- bindin
Albumin.....	50-65	4.9	5.9	4.6	5.9	69 000	Colloid pressure and res protein
Acid α_1 -glycoprotein (α_1 - seromucoid, orosomucoid)	0.5-1.5	2.7	5.1	3.1	5.3	44 100	Tissue- down 1 (?)
α_1 -Antitrypsin.....	1.9-4.0	—	—	3.4	—	45 000	Inhibit trypsin
α_2 -Macroglobulin.....	1.5-4.5	5.4	4.2	19.4	2.4	900 000	Inhibit protein
α_2 -Haptoglobin.....	0.3-1.9	4.1	3.3	4.1	4.7	85 000	Haemo- binding
α_2 -Caeruloplasmin.....	0.3-0.5	4.4	4.6	7.2	4.7	150 000	Oxidase (?); cop content
β_1 -Siderophilin (transferrin)	3.0-6.5	5.8	3.1	6.1	6.2	88 000	Iron tra defence infectio
α_1 -Lipoprotein density 1.093.....	} 4.5-8	—	—	{ 5.5	—	435 000	} Lipid tr
density 1.149.....				{ 5.0	—	195 000	
α_2 -Lipoprotein.....	0.5-1.5	—	—	$S_f > 12$	—	3 400 000	Lipid tr
β_1 -Lipoprotein.....	4-14	5.4	3.1	$S_f = 0-12$	—	2 500 000	Lipid tr
γ A, IgA (β_2 A-globulin, γ_{1A} -globulin).....	0.8-2.8	—	-2.2	7 (10, 13, 15, 17)	—	180 000- 500 000	Immune lins: car of specif humoral bodies**
γ M, IgM (β_2 M-globulin, γ_{1M} -globulin, γ_1 -macroglobulin, 19S γ)..	0.6-1.7	—	-2	18-20	—	950 000	
γ G, IgG (γ -globulin, γ_2 -globulin, γ_{4S} -globulin, 7S γ).....	13-22	7.3	-0.8	6.5-7	4.0	150 000	
γ D, IgD.....	<0.5	—	—	6-7	—	150 000 (?)	
γ E, IgE**.....	<0.002	—	—	8	—	200 000	
Fibrinogen.....	2.5-5.0	5.4	2.1	8.5	2.0	340 000	Coagula

* pH 8.6; ionic strength 0.1.

** Identical with IgND.

[†] From summaries in HIRTZIG, W.H., *Die Plasmaproteine in der klinischen Medizin*, Springer, Berlin, 1963, page 45; PHELPS and PUTNAM, in PUTNAM, F.W. (Ed.), *The Plasma Proteins*, vol. 1, Academic Press, New York, 1960, page 143; WUHRMANN and MARKI, *Dysproteinämien und Paraproteinämien*, Schwabe, Basle, 1963, page 55; SCHWICK and STÖRIKO, *Laboratoriums-Blutchemie*, Bohnenberger AG., Marburg-Lahn.

*** Some of the antibodies in this group are:

γ A Various insulin antibodies, tetanus antitoxin, polio I/III and certain isoagglutinins

γ M Isoantibodies anti-A and anti-B, agglutinating Rh antibodies and nonspecific cold-agglutinins, heterophilic agglutinins, MANN antibodies, antinuclear antibodies, rheumatoid factor (properdin)

γ G Incomplete Rh antibodies, incomplete antibodies anti-A and LE-factor (?), blocking antibodies

γ D Nature unknown

ture of the immunoglobulins?

Structure of the immunoglobulins														
Chains*	H		γ		α		δ		ε		μ		λ	
	L	K	L	K	L	K	L	K	L	K	L	K	L	
Molecular type	K ₂ Y ₂		L ₂ Y ₂		K ₂ α ₂		L ₂ α ₂		K ₂ δ ₂		L ₂ δ ₂		K ₂ λ ₂	
Chain combination	[κ ₂ α ₂] _n		[λ ₂ α ₂] _n		[κ ₂ δ ₂] _n		[λ ₂ δ ₂] _n		[κ ₂ ε ₂] _n		[λ ₂ ε ₂] _n		[κ ₂ λ ₂] _n	
					n = 1, 2, 3						n = 5			
Normal immunoglobulin	γG-Globulin		γA-Globulin		γD-Globulin		γE-Globulin		γM-Globulin		γU-Globulin			
Paraprotein**	Myeloma globulins										Macroglobulin		Bence-Jones globulin	

** Paraproteins are proteins of abnormal structure in the immunoglobulin group appearing in neoplastic diseases of the reticuloendothelial system

* Hesse, K., in *Das gelbe Heft, Immunbiologische Informationen der Bundesgesundheitsbehörde*, 1966, 10, 1-10

amino-acid and carbohydrate composition of human serum proteins (g/100 g protein)¹

	Pre-albumin	Albumin	Acid α ₁ -glycoprotein	α ₂ -Antitrypsin	Haptoglobin	Ceruloplasmin	α ₂ -Macroglobulin	Transferrin	γG-Globulin	γM-Globulin	γA-Globulin
Lysine	6.96	10.95	4.48	7.13	8.17	3.84	3.34	9.65	6.96	4.88	4.57
Histidine	3.62	3.17	1.12	2.92	3.12	3.93	2.70	3.33	2.28	1.83	1.93
Asparagine	1.00	0.94	1.49	1.04	1.40	1.40	1.37	1.23	1.46	1.23	2.02
Arginine	4.27	3.38	3.44	1.83	2.23	4.38	3.82	3.15	4.02	3.05	4.53
Aspartic acid	6.44	9.05	5.72	8.02	9.53	9.43	7.16	11.40	7.69	7.12	6.13
Threonine	9.17	4.31	4.02	4.97	4.42	3.35	3.35	3.71	7.18	7.23	7.63
Serine	7.36	3.15	1.44	2.98	3.50	3.64	3.50	4.38	9.69	6.95	7.93
Glutamic acid	10.91	15.85	10.50	10.90	9.70	10.88	12.30	10.22	11.26	10.62	10.32
Proline	5.31	3.65	1.81	2.69	4.19	3.21	4.07	3.82	6.03	3.27	6.26
Glycine	3.94	1.05	1.03	2.03	2.90	2.98	2.75	3.44	3.33	3.06	3.22
Alanine	6.25	6.67	1.52	2.89	3.53	2.44	3.44	5.00	3.18	3.31	3.87
Cystine ^{1/2}	0	5.09	0.68	0	2.05	0.72	1.14	3.07	2.20	1.58	2.10
Valine	8.44	6.17	2.14	3.86	6.25	4.10	6.80	3.40	8.10	6.49	6.00
Methionine	0.84	1.08	0.37	1.66	1.04	1.98	1.53	1.51	0.85	1.16	0.80
Isoleucine	3.68	1.31	2.46	3.32	3.38	4.13	3.09	2.10	2.14	2.70	1.74
Leucine	5.50	10.30	3.92	8.25	6.03	5.51	7.76	8.21	7.21	6.33	7.76
Tyrosine	5.51	4.03	4.08	1.87	5.55	7.55	4.84	4.61	5.97	4.21	4.38
Phenylalanine	5.11	6.74	3.31	6.37	2.36	5.07	5.37	5.07	4.29	3.96	3.66
Tryptophan	2.40	0.13	1.40	0.55	2.60	2.30	1.30	2.10	3.83	2.80	3.30
Sum	96.73	99.02	54.93	73.32	81.95	84.86	85.63	95.20	97.71	85.98	88.41
Hexoses	0.4	0.05	14.70	4.70	7.80	3.00	3.6	2.40	1.10	5.40	3.20
Acetylhexosamine	0.1	0.03	13.90	3.90	5.30	2.40	2.9	2.00	1.30	4.40	2.90
Acetylneuraminic acid	0	0	12.10	3.60	5.30	2.40	1.8	1.40	0.30	1.30	1.80
Tucose	0	0	0.70	0.20	0.20	0.18	0.1	0.07	0.20	0.70	0.22
Sum	97.23	99.10	96.33	85.72	100.55	92.84	94.03	101.07	100.61	97.78	96.53

¹ HIRSHMAN ET AL., *Clinical Acid*, 10, 293 (1964)

Serum and plasma protein fractions of adults

Free electrophoresis of serum and plasma proteins¹

	Serum (30 subjects)						Plasma (7 subjects)			
	Absolute values (g/l serum)			Relative values (g/100 g total protein)			Absolute values (g/l plasma)	Relative values (g/100 g total protein)		
	Mean	Extreme range	s	Mean	Extreme range	s	Extreme range	Mean	Extreme range	
Total protein.....	73	68-82	3.7	100	-	-	~69-85	100	-	
Albumin	46.2	42.2-53.9	2.9	63.5	59.7-68.6	2.32	-	61.2	57.0-65.8	2
Globulins	26.8	22.5-31.0	2.2	36.5	31.4-40.3	2.32	-	38.8	32.2-43.0	3
α-Globulin	6.8	5.1-9.8	1.1	9.2	7.0-12.2	1.43	-	9.2	8.1-10.5	6
α ₁ -Globulin....	-	-	-	2.0	1.1-3.0	0.52	-	-	-	
α ₂ -Globulin....	-	-	-	7.3	5.5-9.8	1.15	-	-	-	
β-Globulin	8.2	5.5-10.1	1.1	11.3	7.7-14.0	1.40	-	11.5	10.5-12.9	1
γ-Globulin	11.6	8.8-15.0	1.4	15.9	12.3-18.9	1.6	-	14.1	12.7-17.0	1
Fibrinogen	-	-	-	-	-	-	~2-4	4.0	2.2-5.8	1
Albumin: globulin ratio	-	-	-	1.74	1.49-2.19	0.17	-	1.59	1.32-1.92	0.

¹ RIVA, G., *Das Serumweißbild*, 2nd ed., Huber, Berne, 1960, page 257.Electrophoresis of serum proteins on paper¹ or cellulose acetate²

	Paper electrophoresis (12 subjects)			Electrophoresis on cellulose acetate (40 subjects)			
	Relative values (g/100 g total protein)			Absolute values (g/l serum)		Relative values (g/100 g total protein)	
	Mean	Extreme range	s	Mean	95% range	Mean	95% range
Total protein.....	100	-	-	75.0	66-84	100	-
Albumin	65.2	58.0-71.9	4.35	44.7	37-52	59.6	52.2-67.0
Globulins	34.8	28.1-42.0	4.35	-	-	-	-
α-Globulin	10.9	8.4-14.2	2.0	-	-	-	-
α ₁ -Globulin....	4.1	3.1-6.6	1.14	2.5	1-4	3.5	2.4-4.6
α ₂ -Globulin....	6.7	5.2-9.1	1.28	7.5	5-10	10.1	6.6-13.6
β-Globulin	9.8	6.1-12.0	1.64	9.0	6-12	11.9	9.1-14.7
γ-Globulin	14.1	10.3-18.4	2.92	11.1	6-16	14.8	9.0-20.6
Fibrinogen	-	-	-	-	-	-	-
Albumin: globulin ratio	1.92	1.42-2.59	0.38	-	-	1.48	-

¹ RIVA, G., *Das Serumweißbild*, 2nd ed., Huber, Berne, 1960, page 257.² KAPLAN and SAVORY, *Clin.Chem.*, 11, 937 (1965).Serum proteins of men at various ages (g/l)¹

	Num- ber	Total protein		Albumin		α ₁ -Globulin		α ₂ -Globulin		β-Globulin		γ-Globulin	
		Mean	95% range	Mean	95% range	Mean	95% range	Mean	95% range	Mean	95% range	Mean	95% range
18-36 years....	22	71.9	62.1-81.7	38.1	29.9-46.3	3.7	2.3-5.4	7.6	3.8-11.3	9.9	6.7-17	12.5	7.3-17
65-92 years....	43	69.3	58.4-89.2	32.7	26.9-38.5	3.8	2.4-5.2	8.8	5.8-11.8	11.3	8.7-13.9	13.0	6.6-19.4

¹ Paper electrophoresis values from National Institute of Mental Health, Bethesda, Maryland, in BIRREN et al. (Eds.), *Human Aging*, Public Health

Service Publication No.986, U.S. Department of Health, Education and Welfare, Bethesda, 1963, page 37.

m proteins at various ages (g/l)

	Reference	Total protein	Albumin*	α_1 -Globulin*	α_2 -Lipoprotein**	α_3 -Globulin*	α_2 -Macroglobulin**	α_2 -Haptoglobulin***	α_2 -Ceruloplasmin*	β -Globulin*	β_2 -Lipoprotein**	β_2 -Sideroprotein*	γ A-Globulin**	γ M-Globulin**	γ G-Globulin**
		Mean (± in brackets)													
Maternal blood	1	59.31 (3.54)	27.46 (3.00)	3.97 (0.71)	2.36 (2.24)	7.30 (1.45)	4.33 (1.45)	1.44 (0.69)	0.89 (0.27)	10.85 (1.26)	4.89 (1.93)	4.80 (0.64)	1.05 -	0.96 (0.46)	10.9 (0.8)
Ord blood, ...	1	54.81 (3.24)	32.16 (3.38)	2.31 (0.31)	0.28 (0.22)	4.51 (0.58)	4.54 (1.44)	0.26 (0.38)	0.11 (0.06)	4.66 (0.86)	1.16 (0.47)	3.33 (0.24)	<0.02 -	<0.09 -	12.5 (2.0)
Children															
0-14 days ...	1	51.30 (5.10)	30.06 (3.64)	2.33 (0.39)	0.65 (0.27)	4.89 (0.62)	5.17 (1.12)	0.15 (0.07)	0.17 (0.05)	4.32 (0.79)	2.50 (0.74)	2.70 (0.09)	<0.02 -	0.22 (0.06)	9.9 (0.8)
2-4 weeks	1	50.78 (3.74)	29.71 (3.54)	2.59 (0.66)	0.40 (0.17)	4.86 (1.16)	4.55 (2.70)	0.41 (0.37)	0.20 (0.08)	5.01 (0.75)	1.38 (0.43)	2.74 (0.26)	0.09 (0.12)	0.27 (0.09)	9.5 (0.6)
5-9 weeks	1	53.37 (3.04)	35.10 (2.64)	2.60 (0.49)	0.33 (0.15)	5.13 (0.82)	3.60 (1.70)	0.25 (0.24)	0.24 (0.06)	5.25 (0.61)	1.42 (0.46)	3.03 (0.23)	0.43 (0.25)	0.26 (0.11)	6.3 (1.8)
2-6 months	1	56.50 (3.98)	35.02 (2.78)	2.01 (0.72)	0.61 (0.31)	6.78 (1.15)	5.44 (1.81)	0.73 (0.41)	0.25 (0.11)	6.75 (1.27)	2.36 (1.03)	3.59 (0.35)	0.50 (0.20)	0.35 (0.13)	5.8 (1.2)
6-13 months	1	60.56 (3.31)	36.09 (2.63)	2.19 (0.61)	0.89 (0.39)	7.55 (1.37)	5.60 (2.01)	1.17 (0.57)	0.39 (0.17)	7.81 (0.82)	3.26 (1.03)	3.94 (0.38)	0.69 (0.27)	0.55 (0.23)	7.5 (1.5)
1½-3 years	2	64.40 (4.31)	36.20 (3.39)	3.26 (0.72)	-	8.15 (1.27)	5.00 (1.41)	0.95 (0.46)	0.51 (0.09)	8.92 (1.38)	4.60 (1.71)	3.53 (0.41)	-	0.67 (0.36)	8.66 (2.42)
3-7 years	2	66.90 (4.56)	36.58 (2.59)	3.40 (0.65)	-	7.59 (1.08)	4.72 (1.27)	0.68 (0.32)	0.51 (0.12)	8.89 (0.23)	4.22 (1.73)	3.53 (0.44)	-	0.64 (0.18)	13.00 (2.81)
7-11 years	2	68.86 (2.64)	37.96 (2.60)	3.15 (0.53)	-	7.15 (1.18)	4.50 (1.50)	0.61 (0.41)	0.44 (0.14)	8.78 (1.50)	4.12 (1.66)	3.57 (0.56)	-	0.61 (0.25)	14.20 (2.71)
11-16 years	2	69.17 (2.79)	37.50 (2.11)	3.32 (0.56)	-	6.81 (0.96)	3.46 (0.87)	0.47 (0.30)	0.41 (0.11)	8.94 (1.56)	3.78 (1.48)	3.41 (0.37)	-	0.55 (0.25)	13.85 (1.83)
Adults	2	69.86 (1.43)	36.58 (2.81)	3.11 (0.41)	-	6.76 (1.27)	2.92 (0.98)	0.81 (0.46)	0.38 (0.08)	8.74 (1.07)	3.56 (1.90)	3.00 (0.38)	-	0.68 (0.29)	13.14 (2.02)
Adults	1	69.25 (1.86)	35.75 (2.11)	3.58 (0.58)	0.80 (0.36)	7.08 (0.96)	3.56 (0.98)	1.10 (0.30)	0.32 (0.08)	8.66 (1.07)	2.18 (1.48)	3.66 (0.37)	0.80 -	0.66 (0.25)	11.7 (1.83)

Within the cell the enzymes are located in various compartments: namely the cytoplasm, mitochondria, lysosomes, microsomes, nucleus, and are classified into types I and II. Type I enzymes are easily extractable and probably only loosely bound to the hy-

Blood - Enzymes

(For references see pages 585-58)

Table 2 Correction factors for conversion of activity values to 25°C

Temperature of measurement	Lactate dehydrogenase ⁴⁴	Alanine aminotransferase ⁴⁴	Aspartate aminotransferase ⁴⁴	Maltate dehydrogenase ⁴⁴	Glucose-6-phosphate dehydrogenase and phosphoglucomutase ⁴⁴	Cholinesterase ⁴⁴
20°C	1.470	1.400	1.390	1.520	1.300	1.360
21°C	1.350	1.310	1.300	1.390	1.240	1.280
22°C	1.250	1.220	1.220	1.280	1.180	1.200
23°C	1.160	1.140	1.150	1.180	1.120	1.120
24°C	1.080	1.060	1.070	1.090	1.060	1.055
25°C	1.000	1.000	1.000	1.000	1.000	1.000
26°C	0.928	0.930	0.936	0.920	0.950	0.950
27°C	0.862	0.874	0.878	0.860	0.900	0.900
28°C	0.802	0.817	0.821	0.800	0.850	0.855
29°C	0.742	0.767	0.770	0.740	0.800	0.815
30°C	0.694	0.716	0.719	0.680	0.760	0.775
31°C	0.640	0.672	0.675	0.630	0.720	0.740
32°C	0.598	0.628	0.636	0.580	0.680	0.700
33°C	0.556	0.591	0.599	0.540	0.650	0.670
34°C	0.520	0.553	0.560	0.500	0.620	0.635
35°C	0.485	0.516	0.523	0.460	0.590	0.605
36°C	0.449	0.484	0.497	0.430	0.560	0.575
37°C	0.419	0.459	0.465	0.400	0.530	0.545

increased release of enzymes during muscular work is more important²⁷.

Physiological variations in enzyme activity (see also the main table on pages 590-600)

The concentrations of the various enzymes in the body fluids have lognormal rather than normal distributions; for this reason the data in the main table do not include the usual 95% range calculated from the mean and standard deviation.

transferase²⁷ and creatine kinase²². For almost all the diagnostically useful enzymes, however, men and women can be assumed to have the same normal limits^{27, 28}.

Age differences. Many enzymes have higher serum values in the immediate postnatal period and early infancy. In the 2nd to 3rd

plasma, like lactate dehydrogenase and alanine aminotransferase, whereas type II enzymes are released only when the cell is severely damaged.

age²⁶, though these are probably a result of the increased incidence of subclinical ailments.

Daily variations. Data on diurnal changes in serum enzyme levels are conflicting. Fluctuations of up to 40% (though with very wide

Table 3 Enzyme activities (in U/g tissue^{44, 45} or U/10¹¹ cells⁴⁴)

Tissue	Hexokinase	Idolol dehydrogenase	Ketose-1-phosphate aldolase	Fructose-1,6-phosphate aldolase	Glycerol-3-phosphate dehydrogenase	Alcohol dehydrogenase	Glycerol-3-phosphate dehydrogenase	Phosphopyruvate hydratase	Pyruvate kinase	Lactate dehydrogenase	Maltate dehydrogenase	Isocitrate dehydrogenase	Glutamate dehydrogenase	Aspartate aminotransferase	Alanine aminotransferase	Glucose-6-phosphate dehydrogenase	Phosphoglucomutase	Phosphorylase kinase	Phosphorylase phosphomutase
Liver	25.2	71.9	3.4	5.7	14.8	30.5	75.2	22.2	15.5	156	202	36.2	60.2	96.0	58.7	0.93	1.39	217	134
Skeletal muscle	3.5	0.01	0.9	98.1	2.5	0.01	175	21.4	67.6	148	93.8	6.8	0.5	36.7	3.4	0.01	0.01	33.8	35.0
Cardiac muscle	2.0	0.01	0.3	5.0	0.6	0.01	62.6	1.7	29.0	125	482	5.2	1.1	52.5	3.0	0.2	0.1	0	0
Uterus	2.2	0.01	0.01	0.9	0.01	0.01	37.5	2.7	11.1	25.6	35.8	1.1	1.1	4.1	0.9	0.9	0.01	15.0	23.1
Stomach muscles	2.3	0.01	0.1	2.6	0.05	0.01	57.4	5.2	17.6	54.1	49.8	2.8	0.7	4.3	0.05	0.5	0.1	0	0
Gastric mucosa	1.7	1.2	0.05	1.1	0.1	0.9	69.8	6.4	22.2	65.7	113	11.0	3.0	28.9	1.1	0.7	0.3	0	0
Pancreas	0.4	0.2	0.09	0.04	0.04	0.1	37.7	3.5	9.8	30.8	47.7	1.8	0.5	3.0	0.7	0.4	0.2	0	0
Renal cortex	2.1	3.6	0.5	1.8	2.4	0.01	108	9.1	15.6	114	105	6.1	6.7	10.6	2.0	0.7	0.5	0	0
Renal medulla	1.1	0.4	0.1	0.7	0.2	0.05	57.8	3.5	23.5	101	49.2	4.4	2.2	8.2	0.7	0.3	0.3	0	0
Cerebral cortex	9.2	0.2	0.1	5.5	0.09	0.01	69.3	10.5	28.5	54.6	117	0.8	4.1	20.3	0.1	0.3	0.3	0	0
Cerebrum	10	0.2	0.64	2.5	0.2	0.01	69.1	7.7	27.9	40.1	61.9	0.9	2.3	9.3	0.01	0.2	0.1	0	0
Cerebellar hemispheres	1.8	0.1	0.77	4.7	0.01	0.01	49.7	12.4	34.9	64.7	78.4	0.2	1.5	21.6	0.07	0.3	0.3	0	0
Lungs	5.4	1.6	0.04	0.5	0.1	0.3	27.5	2.6	8.6	27.4	27.3	1.1	2.5	1.1	0.3	0.6	0.5	0	0
Fatty tissues	0.7	0.01	0.1	1.6	4.5	0.2	19.4	1.6	3.8	52.8	72.7	1.7	1.3	5.2	1.9	1.5	1.2	0	0
Lymph glands	3.7	0.2	0.09	3.4	0.1	0.2	75.5	10.8	30.4	84.0	69.7	4.1	2.7	7.4	0.07	0.9	0.5	0	0
Erythrocytes	2.0	0	0	15.3	0	0	104	18.9	32.8	173	125	1.2	0	6.8	1.4	13.2	7.1	289	64.2
Islets	15	0	0	14.9	19	0	284	30.3	25.3	357	304	2.7	0	14.3	13	28.5	8.2	600	75.4
Thrombocytes	45	0	0	8.2	1.2	0	39.0	23.6	120	97.7	37.2	3.3	0.7	1.6	0.8	6.9	0.9	82.7	39.4
Granulocytes	1.4	0	0	4.6	15.9	0	5.7	5.30	368	9.92	2.43	163	23.8	271	82.3	926	342	11.7	4.16

Table 4 Enzyme concentration gradients⁴

	Skeletal muscle/serum	Liver/serum
Fructosediphosphate aldolase	21 800:1	2700:1
Pyruvate kinase	6200:1	1400:1
Lactate dehydrogenase	1400:1	1400:1
Malate dehydrogenase	2000:1	2600:1
Aspartate aminotransferase	5700:1	9000:1
Alanine aminotransferase	750:1	7600:1

variance in the values) between maximum nocturnal and minimum noon levels have been reported³⁷ as well as marked constancy throughout the day³⁸.

Muscular work. Heavy muscular work causes a marked rise in serum enzyme activities. In untrained test subjects, long-continued work resulted in considerable increases in the levels of aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, fructosediphosphate aldolase, malate dehydrogenase, pyruvate kinase and creatine kinase^{27, 39-41}, the last-named enzyme being markedly sensitive even to quite mild physical exertion^{39, 42}. Alkaline and acid phosphatases, as well as amylase, show no change³³.

Pregnancy. During uneventful pregnancy the serum activities of many enzymes - for instance aspartate aminotransferase, alanine aminotransferase, fructosediphosphate aldolase, isocitrate dehydrogenase, malate dehydrogenase and α -hydroxybutyrate dehydrogenase - remain within the normal range⁴³⁻⁵⁰. There have been reports of irregular increases in aspartate aminotransferase⁴⁷, creatine kinase⁴⁹ and especially lactate dehydrogenase^{47, 48, 51} during the last weeks of gestation, but these have not been confirmed by other workers^{44-46, 52}.

A number of hydrolytically active enzymes (alkaline phosphatase^{45, 47, 53}, leucine aminopeptidase^{50, 54}, oxytocinase⁵⁵, β -glucuronidase^{50, 56}) as well as histaminase⁵⁷ show increases up to many times the normal serum value during pregnancy, with a subsequent return to normal in a few days post partum.

Serum enzyme activities

Most of the diagnostically useful enzymes except those concerned in blood coagulation are best determined in the serum since in the plasma their activity may be inhibited by the presence of added citrate, oxalate, heparin, fluoride, etc.³³. Even slight haemolysis interferes with the determination of the enzymes present at high activities in the erythrocytes, such as lactate dehydrogenase, glucose-6-phosphate dehydrogenase, phosphogluconate dehydrogenase, fructosediphosphate aldolase, arginase, etc., but it can be tolerated in the case of enzymes whose serum and erythrocyte concentrations differ by much less, such as aspartate aminotransferase, alanine aminotransferase, glutamate dehydrogenase, ketose-1-phosphate aldolase, etc.

In general, determinations should be carried out immediately after collection of the serum sample since enzymes may be unstable in the serum. Most of the diagnostically useful enzymes, however, show little change in activity during the first 24 hours if the serum is kept at +4 °C or even room temperature^{33, 34}. Exceptions are glucose-6-phosphatase, glucose-6-phosphate dehydrogenase, phosphogluconate dehydrogenase and creatine kinase³³. For methods of enzyme determination see the literature^{33, 68}.

Elimination of enzymes from the serum

The serum levels of enzymes normally remain fairly constant. Injection of enzymes into the blood is followed by a rapid return to normal values⁵⁹⁻⁶². The reduction takes place in two phases⁶¹, a faster phase of distribution over the whole intercellular space and a slower one of actual elimination. The half-lives in human serum, so far known only approximately, of various enzymes are⁶³⁻⁶⁶: aspartate aminotransferase 46-58 hours, alanine aminotransferase 63-88 hours, lactate dehydrogenase ca. 52 hours.

The mechanism of elimination remains obscure. Alkaline phosphatase and leucine aminopeptidase are excreted in the bile, amylase, pepsinogen and other enzymes of low molecular weight in the urine. Nevertheless, the rates of excretion of yet other enzymes like

aspartate aminotransferase, alanine aminotransferase and lactate dehydrogenase remain unchanged by bilateral nephrectomy, partial nephrectomy or by splenectomy^{59, 61, 63, 67}. The reticuloendothelial system may play an important part in enzyme elimination from blood⁶⁸.

Diagnostic use of enzymes

Maintenance of the normal difference between the enzyme concentrations in the cells and serum is a process closely linked with energy metabolism of the cell. Impairment of energy production as in injury to the cell - results in movement of enzymes out of the cell^{59, 60, 69}, the rate depending on the concentration gradient, molecular weight and location of the particular enzyme. The relative importance of these factors varies with the severity of the injury to the cell. When it is acute and severe - as in cardiac infarction - the enzyme pattern of the organ appears in the serum, whereas in less acute and less severe injury the increase in serum enzyme activity is mainly accounted for by the readily extractable cytoplasmic enzymes; in the latter case the characteristic enzyme pattern is effaced as a result of the different rates at which the enzymes are eliminated^{41, 70-72}.

The extent to which the serum enzyme activity increases in response to the severity and scope of the cell injury^{64, 66, 73}. The seat of the disease can be established by identifying the typical enzyme pattern of the organ in the serum, or by determining 'organ-specific' enzymes or tissue-specific isoenzyme distributions⁷⁴.

Of the many enzymes present in the serum only a few have proved to be of lasting diagnostic value. In order of practical importance these are: aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, acid phosphatase, amylase, creatine kinase, glutamate dehydrogenase, lactate dehydrogenase (and its isoenzymes), iditol dehydrogenase and fructosediphosphate aldolase. Enzyme determinations now play an indispensable part in the diagnosis of liver, heart, muscle and pancreatic diseases.

1. Liver disease. In acute hepatitis there is an increase in most of the serum enzymes so far studied⁷⁵. Aspartate aminotransferase activity rises 10-150 times, that of alanine aminotransferase 20 times. The increase in alkaline phosphatase activity is comparatively small and reflects the accompanying biliary obstruction⁷⁶. There is a decrease in the plasma cholinesterase activity originating in the liver⁷⁷. The increase in enzyme activity precedes the rise in bilirubin concentration and thus allows diagnosis of hepatitis in anicteric patients⁷⁸. The course of the disease can readily be followed with the aid of enzyme determinations, an aggravation or relapse always being manifested by a renewed rise in the serum enzyme levels⁷⁶. Failure of the aminotransferase activities to return to normal in spite of apparent clinical healing is an indication that hepatitis persists in a subchronic form⁷⁶.

A smaller rise in serum aminotransferase activities (2-8 times the normal) occurs in active chronic hepatitis and cirrhosis of the liver^{76, 79-81}. In cases of long standing the aspartate aminotransferase level is usually higher than the alanine aminotransferase level with a fairly marked rise in glutamate dehydrogenase activity. These enzyme changes are quite distinct from those seen in acute hepatitis and are characteristic of the necrotic type of cell injury. Any aggravation of the disease, whether marked by jaundice or not, results in an immediate rise in serum enzyme activities^{76, 79, 81, 82}. In protracted hepatic coma a fall in aminotransferase activity must be regarded as an unfavourable sign^{81, 83-85}; other enzymes - lactate dehydrogenase, malate dehydrogenase, ketose-1-phosphate aldolase, etc. - show large increases in activity⁷⁶.

In the terminal stages of cirrhosis of the liver with ascites the overall enzyme activity shows little pathological change; the aspartate aminotransferase activity is always higher than the alanine aminotransferase activity, however, while glutamate dehydrogenase activity is often detected. These very small increases in aminotransferase activity enable the terminal stages to be distinguished from the so-called 'early' ascites accompanying acute aggravations of the disease, in which aminotransferase activity is very markedly increased owing to the severe injury to the cells⁷⁶.

In adipohepatic liver there are merely slight changes in serum enzyme activities. Marked increases are seen only in very severe fat degeneration or in the presence of secondary inflammation^{76, 86}. Extremely high increases - up to 10 000 U/l for aspartate and alanine aminotransferases and lactate dehydrogenase - occur in acute fatty liver, especially with organic solvents^{64, 87}. A rise in serum enzyme activities following acute alcohol intoxication is seen only in alcoholics and cannot be produced experimentally in healthy persons⁸⁸.

Primary carcinoma of the liver in the presence of cirrhosis of the liver is not marked by any further change in the serum enzyme pattern^{81, 82}. In carcinomatous metastases of the liver there is a moderate overall increase in enzyme activity, with higher aspartate aminotransferase than alanine aminotransferase activity^{72, 73}, and a distinct increase in glutamate dehydrogenase activity⁷⁴, while lactate dehydrogenase levels often exceed 500 U/l^{75, 76}. High alkaline phosphatase values are often also found in the absence of jaundice^{70, 77}.

In obstructive jaundice, diagnostic criteria are the markedly lower increase in aminotransferase activities compared to acute hepatitis^{29, 31, 32} and the rise in alkaline phosphatase³³ and leucine aminopeptidase^{34, 35} activities. Quite often, however, particularly following biliary colic, there are rises in aminotransferase activity like those seen in the milder forms of acute hepatitis^{31, 32, 36}. Another feature often seen is absence of any corresponding increase in alkaline phosphatase activity. The diagnosis can be strengthened by measuring the ratio (aspartate aminotransferase + alanine aminotransferase)/glutamate dehydrogenase³⁷ in inflammatory jaundice liver disease this is over 30, in obstructive jaundice less than 15.

2. *Heart disease.* A rise in serum enzyme activity is a constant (95-100% of patients) and reliable sign of cardiac infarction^{38, 39}. When injury to the cells is acute and short-lived the timely measurement of enzyme activities is particularly important³⁸.

The relatively small mass of muscle damaged in cardiac infarction means that the increase in enzyme activity is markedly less than in acute liver disease. In general, the creatine kinase and aspartate aminotransferase activities reach values 10 times the normal, the lactate dehydrogenase and fructosediphosphate aldolase activities values 3-6 times the normal^{74, 76}. The close correlation between the size of the infarct and the level of serum enzyme activity observed^{39, 40} supports the view that the rise in enzyme activity is due to the release of enzyme from damaged muscle cells. The enzyme pattern in the serum resembles that in the myocardium, namely higher aspartate amino-

Table 5 Serum enzyme activities following cardiac infarction⁷

	Severe to rise at (hours)	Maximum activity at (hours)	Return norm after (d)
Creatine kinase	2-4	24-36	3-6
Aspartate aminotransferase . .	4-6	24-48	4-7
Lactate dehydrogenase	8-10	48-72	8-9
Lactate dehydrogenase isozymes 1 and 2	8-10	24-92	10-12
Fructosediphosphate aldolase	4-6	24-48	2-9

3. *Muscular disease.* After severe muscular injury there is a slight increase particularly in those enzymes with a high activity in muscle, namely creatine kinase, aspartate aminotransferase and fructosediphosphate aldolase. Very marked increases in activity are observed in muscular dystrophy, especially of the DUCHENNE type¹⁰⁹⁻¹¹²; in other types the rise is distinctly smaller and more irregular¹⁰³⁻¹¹². The extent of the increase in enzyme activity depends on the severity

An increase in serum enzyme activities is also seen in chronic polymyositis^{110, 114, 116}, in dystrophic myotonia^{116, 117, 118} and in dermato myositis; in the latter disease, lactate dehydrogenase and glucose phosphate isomerase are especially prominent, and the aminotransferase activity may reach 400-600 U/l¹¹².

and are indicative merely of primary or secondary involvement of the liver^{38, 112}.

In acute pancreatitis the serum amylase and lipase activities start to rise within 3-6 hours and attain a maximum after 20-30 hours. Increased activities are still observed after 48-72 hours after which

Changes in serum enzyme activity are also associated with various types of tachycardia of frequency exceeding 160/min¹⁰³ and are due to congestion of the liver.

Pulmonary embolism can be distinguished from cardiac infarction

hydrogenase, have not been fulfilled. The frequency with which an increased lactate dehydrogenase activity occurs in patients with tumours varies between 40% and 90%¹²⁹. The values for this enzyme, among 26 whose activities in the serum of patients with tumours of very different kinds were studied, proved to be the most regular in their behaviour¹³⁰. They constitute no reliable index, however, since an increase in the lactate dehydrogenase activity is not a constant observation even when tumours are widely disseminated; it is also a feature of a great many other diseases.

The characteristic enzyme pattern seen in carcinomatous metastases of the liver has already been mentioned.

Apart from the diseases mentioned in this chapter, there are many others in which serum enzyme determinations can play a valuable role in the diagnosis and in following the course of the disease. This is particularly so when measurements are made not on a single enzyme but on a selected group of two, three or more enzymes whose relationship to the other symptoms of the disease has been established⁷⁶.

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Blood – Enzymes

Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets: abbreviation and non-recommended trivial name	Method	Num- ber	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks (see also text on pages 584-
1.1.1.1 Alcohol:NAD oxidoreductase Alcohol dehydrogenase (ADH)	Optical ¹ , modified, 25 °C ...	7	1.8			2	Slight haemolysis does not interfere. Clinical importance not known to now. Markedly increased serum in acute hepatitis and acute liver disease of a severe type ^{2,3} .
1.1.1.8 1-Glycerol-3-phosphate: NAD oxidoreductase Glycerophosphate dehydrogenase (GDH)	Optical ⁴ , modified, 25 °C ...	19	2.7	(1.6-6.6)		2,5	Slight haemolysis does not interfere. Increased in serum in hepatitis and severe liver disease.
1.1.1.14 1-Iditol:NAD oxido- reductase 1-Iditol dehydrogenase (Sorbitol dehydrogenase [SDH])	Optical ⁶ , modified, 24 °C ... Optical ⁷ , modified, 25 °C ... Optical ⁷ , modified, 25 °C ... Optical ⁷ , modified, 37 °C ... Optical ⁷ , modified, 25 °C Adults Cord blood Children	16 12 91 32	0.9 1.1 0.06 0.08		0.1	7 5 8 9	Owing to the low activity of enzyme in the erythrocytes, haemolysis does not interfere. Activity high in liver only. A rise in serum activity is fairly specific for liver damage ^{5,7,9} .
1.1.1.27 1-Lactate:NAD oxido- reductase Lactate dehydrogenase (LDH)	Optical ¹¹ , modified, 24-27 °C Optical ¹² , modified, 25 °C ... Optical ¹¹ , modified, 25 °C ... Optical ¹¹ , modified, room temperature Optical ¹¹ , modified, 25 °C ... Colorimetric (2,4-diphenyl- hydrazine), 37 °C Optical ¹¹ , modified, 25 °C ... Optical ¹¹ , modified, 25 °C ... Optical ¹¹ , modified, 25 °C Adults Cord blood 1 month 2-3 months 4-6 months 6-12 months 2 years 2-16 years Optical ¹¹ , modified, 25 °C Cord blood Optical ¹¹ , modified, 25 °C Premature infants Newborn Infants Children	161 130 180 107 107 209 175 100 29 6 13 12 14 12 24 202 25 19 36 38	225 88 71 100 144 140 306 306 221 217 197 230 145 126 114 49 42	(120-419) (125-379) (36-130) (30-120) (70-240)		12 14 5 6.2 15 16 16 22 28.8 45 118 89 44 41 44 57 45 18 19 19 19 19	Owing to the high activity of enzyme in the erythrocytes, slight haemolysis results in high serum values. Present organs at high activity, so that increase in the serum activity follows severe organic injury of kind. 5 isozymes have been identified in organs and serum. Determination of total lactate dehydrogenase activity is clinically useful for diagnosis of cardiac infarction and differential diagnosis of anaemia and to some extent in disease; for further discussion see the literature ²⁰ . For normal values of the isozyme distribution see JORDAN and WHITE ^{20a} .

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Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets abbreviation and non recommended trivial name	Method	Number	Mean	95% range (extreme range in brackets)	r	Ref- erence	Remarks (see also text on pages 584-588)
[α -Hydroxybutyrate dehydrogenase] (HBDH)	Optical ²¹ , 22, 25 °C Optical ²¹ , 22, 25 °C Optical ²¹ , 22, 25 °C Optical ²¹ , 22, 25 °C Adults Cord blood ..	42 175 100 152 15	90 108 77 76 211	38 23.5 36 30 164	22 17 24 23 25	Not in itself an enzyme but derives from the simple method of determining the electrophoretically fast-migrating isozymes of lactate dehydrogenase ²² . These are present at high activity in heart muscle and brain and oxidize hydroxybutyrate to a much greater extent than the isozymes mainly present in skeletal muscle and liver. For practical purposes the ratio LDH/HBDH equals the ratio total LDH isozymes/heart-muscle spec. 6c LDH isozyme, a normal value in 42 adults ²² 1.40, in 155 adults ²⁷ 1.34
1.1.1.37 L-Malate NAD oxidoreductase Malate dehydrogenase (MDH)	Optical ²⁶ , modified, 25 °C .. Optical ²⁷ , modified, 25 °C .. Optical ²⁸ , modified, 25 °C .. Optical ²⁸ , modified, 25 °C .. Adults Cord blood ..	28 107 88 202	37.9 23.5 71	(17.0-57.3) 3.4 17 18 9 18 10	Owing to the high activity of this enzyme in the erythrocytes even slight haemolysis results in 'false' high serum values. In the neonatal period the upper limit of the normal may be up to 100 U/l ²⁸ . Diagnostic importance so far slight. Present in all organs at high activity, so that an increase in the serum activity follows severe organic injury of any kind, for instance cardiac infarction, liver damage, blood disease. For reviews see the literature ²⁰ .
1.1.1.38 (40) L-Malate NAD(P) oxidoreductase (decarboxylating) Malate dehydrogenase (decarboxylating) (Malic enzyme)	Optical ²⁹ , 25 °C	30	(0-0.5)	20
1.1.1.42 Isocitrate-NADP oxidoreductase (decarboxylating) Isocitrate dehydrogenase (ICDH)	Optical ²¹ , 25 °C Optical ²² , room temperature Optical ²⁷ , modified, 25 °C Adults Cord blood ..	44 38 13 30	2.0 1.3 3.5 3.7	(0.86-4.8) (0.96-1.9) (1.0-7.3) 2.6	21 22 33	Slight haemolysis does not interfere. In cord blood the activity is much higher than in the blood of adults but falls within 10 days ¹⁸ , other studies ²² showed little difference. The serum activity increases in liver damage ² . In cardiac infarction it is rather unchanged ²⁴ or shows only a slight and transient rise ²⁶ .
1.1.1.44 6-Phospho-D-gluconate NADP oxidoreductase (decarboxylating) Phosphogluconate dehydrogenase (decarboxylating) (PGDH)	Optical ²¹ , 25 °C Optical ²⁸ , modified, 25 °C ..	26 17	2.5 1.0	(0.7-4.0)	27 8	Owing to the high activity of this enzyme in the erythrocytes even slight haemolysis results in 'false' high serum values. The serum activity is normal during pregnancy, in cord blood rather higher than in the blood of adults. Diagnostic importance so far small. The activity increases in acute hepatitis ² and blood disease ²⁷ . Its determination in vaginal fluid has been suggested as a test for gynaecological cancer ²⁸ .

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Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets abbreviation and non-recommended trivial name	Method	Num- ber	Mean	95% range (extreme range in brackets)	^a	Refer- ence	Remarks (see also text on pages 584-588)
[α -Hydroxybutyrate dehydro- genase] (HBDH)	Optical ^{22, 23} , 25 °C	42	90			38	Not in itself an enzyme but derives from the simple method of determining the electrophoretically fast-migrating isozymes of lactate dehydrogenase ²⁷ . These are present at high activity in heart muscle and brain and oxidize hydroxybutyrate to a much greater extent than the isozymes mainly present in skeletal muscle and liver. For practical purposes the ratio LDH/HBDH equals the ratio total LDH isozymes/heart-muscle specific LDH isozymes, normal values in 42 adults ²² 1.40, in 155 adults ²⁷ 1.34
	Optical ^{21, 22} , 25 °C	175	108			23.5	
	Optical ²¹ , 22, 25 °C	100	77			36	
	Optical ²¹ , 22, 25 °C						
	Adults	152	76			30	
	Cord blood	15	211			164	
1.1.1.37 L-Malate-NAD oxido- reductase Malate dehydrogenase (MDH)	Optical ²⁶ , modified, 25 °C ..	28	37.9	(17.0-57.3)		8	Owing to the high activity of this enzyme in the erythrocytes even slight haemolysis results in 'false' high serum values. In the neonatal period the upper limit of the normal may be up to 100 U/l ²⁸ . Diagnostic importance so far slight. Present in all organs at high activity, so that an increase in the serum activity follows severe organic injury of any kind, for instance cardiac infarction, liver damage, blood disease. For reviews see the literature ²⁹ .
	Optical ²⁷ , modified, 25 °C ..	107	23.5			3.4	
	Optical ²⁸ , modified, 25 °C ..	88	71			17	
	Optical ²⁸ , modified, 25 °C ..						
	Adults			(12.5-50)		16	
	Cord blood	202		(93.4-265)		18	
1.1.1.38 (40) L-Malate-NAD(P) oxido- reductase (decarboxylating) Malate dehydrogenase (decarboxylating) (‘Malic’ enzyme)	Optical ²¹ , 25 °C ..	30		(0-0.5)		20	
5.1.1.42 3-keto-DL-isocitrate NADP oxidoreductase (decarboxyl- ating) Isocitrate dehydrogenase (ICDH)	Optical ²¹ , 25 °C ..	44	2.0	(0.85-4.8)		41	Slight haemolysis does not interfere. In cord blood the activity is much higher than in the blood of adults but falls within 10 days ¹⁰ . Other studies ³² showed little difference. The serum activity increases in liver damage ⁹ . In cardiac infarction it is either unchanged ²⁴ or shows only a slight and transient rise ³³ .
	Optical ²² , room temperature ..	38	1.3	(0.96-1.9)		32	
	Optical ²⁷ , modified, 25 °C ..						
	Adults	13	3.5	(1.0-7.3)		8	
	Cord blood	30	3.7			2.6	
1.1.1.43 6-Phospho-D-gluconate NADP oxidoreductase (decarboxylating) Phosphogluconate dehydrogenase (decarboxylating) (PGDH)	Optical ²¹ , 25 °C ..	26	2.5	(0.7-4.0)		31	Owing to the high activity of this enzyme in the erythrocytes even slight haemolysis results in 'false' high serum values. The serum activity is normal during pregnancy, in cord blood rather higher than in the blood of adults. Diagnostic importance so far small. The activity increases in acute hepatitis ^{2, 3} and blood disease ²⁷ . Its determination in vaginal fluid has been suggested ³⁴ .
	Optical ²⁶ , modified, 25 °C ..	17	1.0			6	

Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets: abbreviation and non-recommended trivial name	Method	Num- ber	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks (see also text on pages 581-584)
1.1.1.49 D-Glucose-6-phosphate: NADP oxidoreductase Glucose-6-phosphate dehydrogenase (G-6-PDH) (‘Zwischenferment’ [ZF])	Optical ³⁹ , room temperature Optical ³⁹ , modified, 25 °C .. Optical ³⁹ , modified, 25 °C ..	67 18 38	1.4 1.0 0.24	(0.5–2.4)		32 5 8	Even slight haemolysis r ‘false’ high serum values; activity increased in acute inflammation ⁴⁰ , cardiac infarction ⁴⁰ or severe tissue damage. (Useful when deficiency of enzyme in the erythrocytes suspected (primaquine sen- sitivity as in favism and kernicterus)
1.2.1.12 D-Glyceraldehyde-3-phos- phate:NAD oxidoreductase (phosphorylating) Glyceraldehyde- phosphate dehydrogenase Triosephosphate dehydrogenase (GAPDH)	Optical ⁴² , modified, 25 °C ..	20	7.1	(1.0–11.2)		5	Even slight haemolysis in considerably. Clinical im- portance so far small. Serum activity increased in acute hepatitis ⁴² and mononucleosis ⁴³ and kinds of tumour ⁴⁰ .
1.2.3.2 Xanthine: oxygen oxido- reductase Xanthine oxidase (Hypoxanthine oxidase)	Substrate: 8- ¹⁴ C-xanthine ⁴⁴ , 25 °C	20		(0–0.0005)		44	Clinical importance so far Serum activity increased in damage ⁴⁴ .
1.3.99.1 Succinate: (acceptor) oxido- reductase Succinate dehydrogenase	Optical ⁴⁵			Not detectable		15	Structurally bound enzyme, not detected in serum even in organic injury.
1.4.1.3 L-Glutamate:NAD(P) oxidoreductase (deaminating) Glutamate dehydrogenase (GLDH)	Optical ⁴⁶ , modified, 25 °C ... Optical ⁴⁷ , modified, 25 °C ... Optical (Boehringer), 25 °C .	127 243	1.0 1.0 0.39	< 0.8	0.28	46 47 8	Slight haemolysis does not affect. Largely specific to the Serum activity increased in in- flammatory liver disease and ob- structive jaundice ^{46, 47} , which can be differentiated by means of the (aspartate aminotransferase/) glutamate dehydrogenase ^{47–49} .
1.6.4.2 Reduced-NAD(P):oxidized- glutathione oxidoreductase Glutathione reductase (GR)	Optical ⁵⁰			(5–35)		16	Serum activity markedly incre- ased in acute hepatitis and leukaemia less so in cirrhosis. Also incre- ased in 35–80% of patients with seminated carcinomas ^{51, 52} . In primaquine-sensitive patients, where erythrocytes are poor in glucose- 6-phosphate dehydrogenase, the glutathione reductase activity of cells is doubled ⁵³ .
	Optical ⁵¹ , 25 °C NAD	10	7.0	(3.3–10.2)		51	
	NADP	10	12.6	(4.3–17.4)		51	
	Optical ⁵⁰ , NADP	98	19.2		7.2	52	

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Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name Brackets abbreviation and recommended trivial name	Method	Number	Mean	95% range (extreme range in brackets)	<i>s</i>	Reference	Remarks (see also test on pages 584-588)
caeruloplasmin	Colorimetric (<i>p</i> -phenylenediamine) ⁸⁴ , 37 °C						Caeruloplasmin has the properties of <i>p</i> -diphenol oxidase
	Adults			19-45		10	In pregnancy the caeruloplasmin activity is 2-3 times higher than normal ⁸⁵ . A deficiency of the enzyme is characteristic of hepatolenticular degeneration ⁸⁶ , but is also found in the nephrotic syndrome, kwashiorkor ⁸⁷ and sprue ⁸⁸ . The serum activity is increased in cardiac infarction, infectious diseases, leukaemia, etc. ⁸⁹ .
	Cord blood			3.3-16.7		10	
	1-3 months			12.1-39		10	
	Children			19.2-60		10	
3.3 amoylphosphate L-ornithine carbamoyltransferase	Microdiffusion ⁹⁰ , modified ⁹¹ , 37 °C			(0-0.25)		18	Increased in 25% of normal pregnancies. In cord blood the activity is the same as in normal adults. The observation of an increase in serum activity from the age of 24 years on ⁹² has not been confirmed ⁹³ . The high activity of the enzyme in the liver renders the serum activity a specific index of severe liver damage.
thine carbamoyltransferase	Colorimetric ⁸⁷ , 37 °C			(8-20)		21	
(T)	Isotopic ⁸² , 37 °C ..			(0-0.07)		22	
1.1 heptulose-7-phosphate-L-lysine aldolase	Colorimetric (assay of sedoheptulose 7-phosphate) ⁹⁴ , 37 °C	15	0.82	(0.38-1.42)		66	Serum activity increased in uraemia and often in acute hepatitis, normal in cardiac infarction, cirrhosis of the liver and obstructive jaundice ⁹⁵ .
aldolase		21	0.29	(0.17-0.60)		66	
1.1 aspartate 2-oxoglutarate aminotransferase	Optical ⁹⁷ , 20-22 °C	500	10.6	(2.4-19.2)	3.2	66	Slight haemolysis interferes hardly at all. The clinical importance of this enzyme lies in the marked improvement it has brought about in the diagnosis of cardiac infarction and liver disease. For reviews see the literature ^{96, 97} .
partate aminotransferase	Optical ⁹⁷ , 38 °C	160	16.6		0.4	66	
utamate-oxalacetate transaminase (GOT)	Optical ⁹⁷ , modified, 25 °C	105	8.0	(3.6-17.0)		6	
	Optical (Boehringer), 25 °C, blood donors	950	12.0	(6.2-22.0)		70	
	Optical ⁹⁷ , 25 °C, blood donors	100	13.6		3.2	10	
	Optical ⁹⁷ , 25 °C			(4-15)		10	
	Colorimetric ⁷¹ , modified, 25 °C			(5-18)		18	
	Optical (Boehringer), 25 °C	577	7.67		1.8	6	
	Optical ⁹⁷ , 25 °C						
	Cord blood	44	21.3		9.5	10	
	Up to 1 month	12	20.4		9.7	18	
	2-3 months	13	22.6		6.3	10	
	4-6 months	12	24.3		5.5	10	
	7-12 months	16	19.3		5.4	10	
	2 years	6	15.7		4.8	10	
	2-16 years	58	14.1		3.9	10	
	16 years	49	14.4		4.0	18	
	Cord blood	15	12.6		9.0	28	
	Cord blood	202		(0-20)		18	
	Optical ⁹⁷ , 25 °C						
	Premature infants	25	9.2		9.4	19	
	Newborn	20	8.8		4.5	19	
	Infants	41	4.8		2.6	19	
	Children	43	3.7				

Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets: abbreviation and non-recommended trivial name	Method	Num- ber	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks (see also text on pages
2.6.1.2 L-Alanine:2-oxoglutarate aminotransferase Alanine aminotransferase (Glutamate-pyruvate-trans- aminase [GPT])	Optical ⁷³ , modified, room temperature	54	3.7		2.1	⁷⁴	Slight haemolysis does fere. High activity in li- cally none in erythrocy- activity increased marks disease, in the diagnosis is the most important e- reviews see the literatur
	Optical ⁷³ , 20-22 °C	260	7.7	(2.4-16.8)		⁷³	
	Optical ⁷³ , modified, 25 °C ..	122	6.9	(2.9-16.1)		⁵	
	Optical (Boehringer), 25 °C, blood donors	2400		(6.4-16.0)		⁷⁰	
	Optical ⁷³ , 25 °C, blood donors	2400		(6.4-16.0)		⁷⁵	
	Optical (Boehringer), 25 °C .	722	5.54		1.7	⁸	
	Cord blood	44	5.0		2.3	¹⁰	
	1 month	11	4.0		3.0	¹⁰	
	2-3 months	11	7.5		1.6	¹⁰	
	4-12 months	14	6.2		2.7	¹⁰	
	From 1 year	31	6.8		3.3	¹⁰	
	Cord blood	202		0.5-9.6		¹⁸	
2.7.1.1 ATP:D-hexose 6-phospho- transferase Hexokinase (HK)	Optical, with glucose 6-phos- phate dehydrogenase, 25 °C	30		Not detectable		¹⁵	Haemolysis interferes. I usefulness so far. Serum creased in acute hepatitis
	Optical, 25 °C	7	0.1			⁵	
2.7.1.3 ATP:D-fructose 1-phospho- transferase Ketohexokinase (Fructokinase [FK])	Optical ⁷⁶ , modified, 25 °C ..	30		Not detectable		³⁰	No clinical usefulness so activity increased in ac- tis ³⁰ .
2.7.1.40 ATP:pyruvate phospho- transferase Pyruvate kinase (PK)	Optical ⁴² , modified, 25 °C ..	19	16.4	(3.8-34.8)		⁵	No clinical significance. hepatitis the serum activ- a non-significant reducti- bed-res ⁷² ?, in patients mouts an increase ³⁰ . spherocytic haemolytic ar- erythrocytes have been be deficient in this enzyme
	Optical ⁴²	20	29.9	(15.7-49.6)		⁷⁷	
	Optical ⁴² , modified, 25 °C ..	30	15.8		6.0	³⁰	
2.7.2.3 ATP:3-phospho-D-glycerate 1-phosphotransferase Phosphoglycerate kinase (PGK)	Optical ⁴ , modified, room temperature	107	11.2		3.1	¹⁵	Serum activity increased mia ¹⁵ . In cardiac infar- acute hepatitis normal ¹⁵ higher values ⁴⁹ have bee
2.7.3.2 ATP:creatine phospho- transferase Creatine kinase (Creatine phosphokinase [CPK])	Colorimetric ⁷⁹ , 37 °C			(3.3-23.7)		⁷⁹	Slight haemolysis does fere. Higher serum acti- found following physical ⁸⁵ . In men the normal slightly higher than in wo- Creatine kinase is a sensiti- in the diagnosis of car- muscular diseases. For re- the literature ²⁰ .
	Colorimetric ⁸⁰ , 37 °C			(5.5-75)		⁸¹	
	Optical ⁸² , 37 °C	254	0.40		1.3	⁸³	
	Optical (Boehringer), 25 °C .	257	0.30	< 1.0	0.30	⁸	
	Optical (Boehringer), 25 °C .	30		(0-0.48)		⁸⁴	
	Optical ⁸² , 37 °C						
	Adults		1.0		0.8	²⁵	
	Cord blood		2.1		1.8	²⁵	
	Pregnancy, 3rd trimester ..		2.9		5.6	²⁵	

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Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets abbreviation and non-recommended (trivial) name	Method	Num- ber	Mean	95% range (extreme range in brackets)	#	Refer- ence	Remarks (see also text on pages 584-588)
2.7.4.3 ATP:AMP phosphotrans- ferase Adenylate kinase (Myokinase [MK])	Optical ²² , 25 °C....	25	8.7		31	²⁷	In striped muscle the absolute activity of adenylate kinase is higher than that of creatine kinase ²⁸ . Occurs at relatively high activities in leucocytes and thrombocytes. The usefulness of serum determinations in the diagnosis of cardiac and muscular diseases is limited by the necessity of using serum completely free of haemolysis ²⁷ .
2.7.5.1 α-D-Glucose-1,6-diphosphate α-D-glucose-1-phosphate phosphotransferase Phosphoglucumutase Glucose phosphomutase (PGluM)	Fructose 6-phosphate assay ²⁹ , 37 °C	10	8.3	(1.7-23.4)		²⁹	Slight haemolysis does not interfere. In cord blood, values only half as high as in adults have been found. Little clinical importance. Increased in liver damage ³¹ .
	Fructose 6-phosphate assay ²⁹ , 37 °C	30	9.8		52	³⁰	
	Glucose 1-phosphate assay ³⁰ , 37 °C		9.2	(4-17)	34	³⁰	
3.1.1.3 Glycerol-ester hydrolase Lipase	Titrimetric (substrate olive oil), 37 °C	68	78		29	³²	Haemolysis interferes because of inhibition of the reaction by the haemoglobin. No sex specific differences have been observed ³³ . The marked increase in the serum activity in acute pancreatitis has so far found little diagnostic application ³⁴ . In chronic pancreatitis the changes are not reliable, better results are obtained with provocation tests ³⁵ . Slight increases in serum lipase activity are seen in inflammatory liver diseases ³⁶ .
	Titrimetric (substrate olive oil), 37 °C			(18-285)		³³	
	Titrimetric (substrate phenyl laurate), 37 °C			(9-20)		³⁴	
3.1.1.8 Acetylcholine acyl hydrolase Cholinesterase (ChE)	Colorimetric (acetylcholine bromide), 37 °C			(2000-5200)		³⁷	Slight haemolysis does not interfere. In cord blood the serum activity is very low but becomes normal after the 10th day, after 2 months the value is about 25% higher than in adults. Serum activity is lower in hepatitis and cirrhosis, in accordance with the reduced serum albumin level ¹⁰² . Determination of serum cholinesterase activity has its most important application in detecting poisoning by organic phosphorus compounds (insecticides ¹⁰³) and assessing tolerance to muscle relaxants ¹⁰⁴ . Hereditary deficiency of the enzyme, in which atypical enzyme variants may occur, can be detected by determining the dibucaine numbers.
	Optical (benzoylcholine), 25 °C			(620-1370)		³⁸	
	Colorimetric (phenyl benzoate), 37 °C			(3200-7000)		³⁹	
	Optical (benzoylcholine), 25 °C	60	1026		233	²⁴	
	Colorimetric (acetylcholine), 37 °C	250	1530		333	¹⁰⁰	
	Colorimetric (benzoylcholine), 37 °C	250	1560		333	¹⁰⁰	
	Colorimetric (α-naphthyl propionate), 37 °C	250	3050		466	¹⁰⁰	
	Colorimetric (β-naphthyl propionate), 37 °C	250	1750		383	¹⁰⁰	
	Colorimetric (phenyl acetate), 37 °C	250	16600		3830	¹⁰⁰	
	Colorimetric (monosuccinylcholine), 37 °C	250		< 20		¹⁰⁰	
	Colorimetric (disuccinylcholine), 37 °C	250		< 20		¹⁰⁰	
	Titrimetric (acetylcholine chloride), 37 °C	25	4440		620	¹⁰¹	
	Men (blood donors)	25	3640		680	¹⁰¹	
	Women (blood donors)	25					

	KING ¹⁰⁸	RICHTER ¹⁰⁴
Normal	80 ± 3	62-90
Heterozygotes	62 ± 8	30-60
Atypical homozygotes	22 ± 6	30

Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets: abbreviation and non-recommended trivial name	Method	Num- ber	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks (see also text on pages 584-5)
3.1.3.1 Orthophosphoric monoester phosphohydrolase Alkaline phosphatase	Substrate phenyl phosphate, 37 °C.....			(25-92)		105	Serum activity increased in c hood ^{105, 110} and towards term pregnancy (see page 586). The important application of serum alkaline phosphatase determinati in the diagnosis of liver and b diseases, in the former as indic of the degree of intra- or extra- hepatic biliary obstruction, in the latter as confirmation (when increa of rickets and to a lesser extent osteomalacia. High activities are so seen in bone tumours and in metastases marked by an increase in osteoblasts. For reviews see literature ¹¹³ .
	Substrate p-nitrophenyl phosphate, 37 °C.....			(13.4-38)		106	
	Substrate phenolphthalein phosphate, 37 °C.....			(0.6-4.2)		107	
	Substrate β-glycerophos- phate, 37 °C.....			(15.1-46.4)		108	
	Substrate β-glycerophos- phate, 37 °C.....			(8.2-21.8)		109	
	Substrate p-nitrophenyl phosphate, 37 °C						
	Adults	100	29		8	110	
	Cord blood	15	60		19	110	
	1 month	3	59			110	
	2-3 months	17	98		29	110	
	4-6 months	14	98		32	110	
	7-12 months	15	92		29	110	
	2-15 years	142	88		26	110	
	Substrate phenyl phosphate, 37 °C						
	Newborn			(35-105)		16	
	1 month			(70-250)		16	
	1-3 years			(70-210)		16	
	3-10 years			(70-180)		16	
	10-16 years			(100-275)		16	
	Substrate p-nitrophenyl phosphate, optimum con- ditions ¹¹¹ , 25 °C.....	73	102	61-171		112	
3.1.3.2 Orthophosphoric monoester phosphohydrolase Acid phosphatase	Substrate p-nitrophenyl phosphate, 37 °C						The acid phosphatase of serum originates from various sources (erythrocytes, thrombocytes, leu- kocytes, prostate, bone) which can be identified by the difference in behaviour towards formol and L- tartrate. Serum acid phosphatase determination is important in the diagnosis of prostate carcinoma though in most cases an increase occurs only in the presence of bony metastases. The diagnosis can be established with greater certainty by determining the formol-stable and tartrate-labile fractions, espe- cially the latter. For reviews see the literature ¹¹⁶ .
	Total						
	Serum, men		9.15		4.40	114	
	Serum, women		8.00		2.94	114	
	Plasma, men		5.08		3.54	114	
	Plasma, women		4.41		1.60	114	
	Prostatic						
	Serum, men		1.84		1.80	114	
	Serum, women		1.85		1.58	114	
	Plasma, men		0.32		0.64	114	
	Plasma, women		0.33		0.60	114	
	Substrate phenyl phosphate, 37 °C						
	Formol-stable		4.25			115	
	Tartrate-labile		1.25			115	
	Total		5.5			115	
	Newborn			(3-6)		16	
	1 month			(6.5-11)		16	
	1-3 years			(6.5-11)		16	
	3-10 years			(3.5-9)		16	
	10-16 years			(3-10)		16	

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Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets abbreviation and non-recommended trivial name	Method	Num- ber	Mean	95% range (extreme range in brackets)	Refer- ence	Remarks (see §10 text on pages 584-588)
3.1.3.5 5'-Ribonucleotide phospho- hydrolase 5'-Nucleotidase	Colorimetric ¹¹⁷ , 37 °C.....			(2-15)	117	Values in children the same as in adults. Like alkaline phosphatase, this enzyme shows a large rise in serum activity in obstructive jaundice ¹¹⁸ and a smaller one in hepatogenic jaundice ¹¹⁹ . Unlike alkaline phosphatase it shows no increase in bone disease ¹¹⁸ .
3.1.3.9 D-Glucose-6-phosphate phosphohydrolase Glucose-6-phosphatase	Colorimetric ¹²⁰ , 37 °C . .		8		120	Haemolysis interferes because of the rise in nonspecific phosphatases. Serum activity increased in acute hepatitis and chronic liver disease ¹²⁰ .
3.1.4.5 Deoxyribonuclease oligo- nucleotidohydrolase Deoxyribonuclease (DNAse, DNase)	Colorimetric, 37 °C . .		0.65	(0-1.8)	121	
3.1.4.6 Deoxyribonuclease 3'-nucleo- tidohydrolase Deoxyribonuclease II (DNase II)	Colorimetric, 37 °C .		0.56	(0-1.2)	121	
3.2.1.1 α-1,4-Glucan 4-glucano- hydrolase α-Amylase	Amylclastic ¹²² , modified, 37 °C	100	1500		615 24	Haemolysis interferes because of inhibition of the reaction by haemoglobin. Serum activity is low in the newborn but rises to the adult level during the first year ²⁴ . It is pathologically increased in acute pancreatitis and pancreatic carcinoma, occasionally also in other abdominal conditions, severe renal failure, and mumps. It is rather lower in chronic pancreatic insufficiency. The most important enzyme in the diagnosis of pancreatic disease. For reviews see the literature ¹²³ .
3.2.1.31 β-D-Glucuronide glucurono- hydrolase β-Glucuronidase	Colorimetric (phenol- phthalate mono-β-D-glucuro- nate), 37 °C Men . Women . Men . Women . Colorimetric (p-nitrophenyl β-D-glucuronate), 25 °C Men . . . Women . . .			(0.2-0.55) (0.09-0.4) 0.62 0.46 0.35-1.32 0.22-0.99	18 19 124 124 124a 124a	Slight haemolysis does not interfere. Serum activity increases in the 3rd trimester of pregnancy but returns to normal post partum (see page 586). High levels are seen in pre-eclampsia ¹²⁵ and carcinoma of the pancreatic head, in other forms of carcinoma the rise is smaller ²⁰ . Serum activity also increased in pancreatitis and liver damage ²⁰ , less so in advanced cirrhosis and disseminated liver . . .

Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets: abbreviation and non-recommended trivial name	Method	Number	Mean	95% range (extreme range in brackets)	s	Reference	Remarks (see also text on pages 584)
3.4.1.1 L-Leucyl-peptide hydrolase Leucine aminopeptidase (LAP)	Colorimetric (substrate L-leucyl- β -naphthylamide), 37 °C	82	16.4	(15-50)	0.67	126	Slight haemolysis does not fere. Values are somewhat low women, though some work regard the difference as clinically insignificant and others ¹³⁰ found no difference. Serum is greatly increased in pregnancy page 586) and in biliary obstruction of extra- or intrabepatic origin increase in carcinoma of the pancreatic head in the absence of obstruction and liver metastases. Slight increase in inflammatory disease and acute pancreatitis.
	Colorimetric (substrate L-leucylglycine), 37 °C					128	
- [Oxytocin-cleaving aminoacylpeptidase] (Oxytocinase)	Colorimetric (substrate L-cystine-bis- β -naphthyl- amide ¹³² or L-cystine-bis- p-nitroanilide ¹³³)						Serum activity increased times in pregnancy (see page 586). The cystine aminopeptidase of normal serum probably due on the leucine aminopeptidase activity ¹³⁴ .
3.4.1.3 Amino-acyl-dipeptide hydrolase Aminopeptidase (Aminotripeptidase)	Colorimetric (substrate glycylglycylglycine), 37 °C	39	64.7		4.2	128	
3.4.4.1 Pepsin	Colorimetric (substrate beef haemoglobin), 37 °C	45	1.72		0.91	135	Formed from pepsinogen. Its activity rather higher in men in women ¹³⁷ . It is low or absent gastric atrophy, increased in presence of duodenal ulcers ¹³
	Colorimetric (substrate beef haemoglobin), 37 °C		2.76	(0.60-8.26)		136	
	1 week		2.41	(1.05-3.08)		136	
	3 weeks-6 years						
3.4.4.4 Trypsin							The serum contains no active trypsin ¹³⁹ . The trypsin-inhibition capacity of 1 ml of serum is sufficient to inhibit on the average 1 unit trypsin.
3.4.4.15 Renin							Formed in the juxtaglomerular apparatus of the kidneys and released into the plasma, where it is involved in the formation of a tensin from angiotensinogen pages 740-741).
3.5.3.1 L-Arginine amidinohydrolase Arginase	Colorimetric ¹⁴⁰ , 37 °C			(0-12)		16	Haemolysis interferes because the high activity of this enzyme the erythrocytes. Serum activity increased in acute and chronic liver injury to the liver parenchyma increase in obstructive jaundice ¹⁴¹ .
3.5.4.3 Guanine aminohydrolase Guanine deaminase (Guanase)	Optical ¹⁴² , 37 °C			0-3		143	Haemolysis does not interfere serum activity increased in liver disease.

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Enzymes: Normal values in U/l plasma or serum of adults unless otherwise stated (for definition of the unit U see page 584)

EC number Systematic name Recommended trivial name In brackets: abbreviation and non-recommended trivial name	Method	Num- ber	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks (see also text on pages 584-58)
4.2.1.11 2-Phospho-D-glycerate hydro-lyase Phosphopyruvate hydratase (Enolase [ENO])	Optical ⁴² , modified, 25 °C .. Optical ⁴² , 25 °C	15 30	3.1 10.5	(1-6.0)	3.3	⁵ ³⁰	Serum activity increased in li hepatitis and progressive muscu dystrophy ^{159,161} , also in gener ized neoplastic disease and esp cially liver metastases ¹⁶⁰ .
5.3.1.1 D-Glyceraldehyde-3-phos- phate ketol-isomerase Triosephosphate isomerase (TIM)	Optical ⁴² , 34 °C	21	142		58	¹⁵⁹	Serum activity increased in vi hepatitis and progressive muscu dystrophy ^{159,161} , also in gener ized neoplastic disease and esp cially liver metastases ¹⁶⁰ .
	Optical ⁴² , 25 °C	30	42.8		15	³⁰	
	Optical ⁴² , modified, 25 °C ..	26	234	(100-400)	58	¹⁶⁰	
5.3.1.6 D-Ribose-5-phosphate ketol- isomerase Ribosephosphate isomerase (Phosphoriboisomerase)	Colorimetric ¹⁶² , 37 °C	11	58.4	(33.4-90.2)		¹⁶²	Serum activity increased in liv disease, nephritis and lymphoma ¹⁶² .
5.3.1.9 D-Glucose-6-phosphate ketol-isomerase Glucosephosphate isomerase (Phosphohexose isomerase [PHI], hexosephosphate isomerase)	Colorimetric ¹⁶³ , 37 °C		50.8		24.2	³⁰	Serum activity higher in earl childhood than in adults. Increase in cardiac infarction ^{165,166} , an acute hepatitis ^{166,167} , slightly s in chronic liver disease and obstruc tive jaundice ^{166,167} . Also increase in leukaemia ¹⁶⁸ , megaloblasti anaemia ⁷⁸ , muscular dystrophy ¹⁶¹ severe thyrotoxicosis ¹⁶⁹ and carci noma ^{167,169,170} .
	Colorimetric ¹⁶⁴ , 37 °C						
	Adults		46.5	(13.5-86.0)		¹⁶	
	Cord blood			(45-170)		¹⁶	
5.4.2.1 D-Phosphoglycerate 2,3-phos- phomutase Phosphoglycerate phosphomutase (PGM)	Optical ¹⁷¹ , modified, 25 °C ..	30		Not detectable		³⁰	No definite changes in serum activ- ity in heart or liver disease or in the presence of tumours ³⁰ .

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Lipids (for references see page 602)

	Erythrocytes				Plasma or serum				Remarks
	Mean	95% range	s	Refer- ence	Mean	95% range	s	Refer- ence	
Total lipids (g/l)	5.10	4.08-6.12	0.51	¹	-	3.5-8.5	-	²	See text opposite.
Fatty acids (g/l)*									
Total	2.0	-	-	¹	-	1.0-5.0	-	²	See text opposite.
Non-esterified ("free")	0.08	-	-	³	-	0.10-0.35	-	²	
Cholesterol (g/l)									
Total	1.20	1.02-1.38	0.09	¹	-	1.0-3.0	-	²	See text opposite.
Free	-	-	-	-	-	0.3-1.0	-	²	

* 1 mmol (mEq)/l \approx 0.28 g/l, or 1 g/l \approx 3.57 mmol (mEq)/l.

	Erythrocytes				Plasma or serum				Remarks
	Mean	95% range	s	Reference	Mean	95% range (extreme range in brackets)	s	Reference	
osphatides (g/l)	2.93	2.58-3.33	0.20	8	-	1.5-3.5	-	8	See text below.
glycerides (g/l)	~0.2	-	-	8	-	0.5-2.2	-	8	See text below
e acids (mg/l)									
hydroxychoholic acid (cholic acid)	1.4	(0-3.4)	-	8	The serum bile acid content is normally less than 10 mg/l ¹⁸ and is increased in diseases resulting in disturbance of bile secretion ¹⁹ , with values up to 400 mg/l.
hydroxychoholic acids (chenodeoxycholic acid and deoxycholic acid)	0.8	(0-1.9)	-	8	

Sal lipids

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etically after suitable extraction⁹

Of the erythrocyte lipids, 90% are contained in the cell membrane. In the leucocytes they account for 5-10% of the dry substance¹⁰, in the thrombocytes about 15%¹¹. The thrombocyte cells have a similar composition to the erythrocyte lipids¹². The rum lipids are mostly bound to proteins (α- and β-lipoproteins, see the tables on page 602). For further discussion of the serum lipids see the literature¹³.

The lipid content of the serum depends on various factors, particularly age, sex, race, diet, hormonal balance, stress, climate, physical exercise and occupation. The serum lipid content is lower at birth and in childhood than in adult life, and rises steadily up to the age of about 60 years, it is increased in pregnancy¹⁴. Its relationship to body weight, constitution and blood pressure has been studied¹⁵. There is a positive correlation between the incidence of atherosclerosis and the lipid (or low-density lipoprotein, cholesterol and glyceride) content of the serum^{16, 17}, though no causal connection has been conclusively demonstrated. The diet should therefore be so adjusted as to avoid an excessive rise in the serum lipid content.

Fatty acids

From about 3% up to about 10% of the serum fatty acids are esterified¹⁸; they consist in the main of components of glycerides, phosphatides and cholesterol esters. Small amounts of free fatty acids are also present in the erythrocytes. Unlike the protein-bound lipids of the other fractions, the free fatty acids of serum are mostly bound loosely as anions to albumin.

The free fatty acid content of the serum rises within a few hours of birth to a level three times as high as that in the cord blood¹⁹. It is rather higher in children before puberty than in adults²⁰, in pregnancy it rises towards term and falls to normal by the second day post partum²⁰.

For the fatty acid content of the lipid fractions see the literature²¹.

Cholesterol

In the serum about one-third of the cholesterol is in the free state, about two-thirds esterified, some 0.7% consists of dihydrocholesterol²². The cholesterol sulphate content of the serum is less than 5 mg/l²³. The ratio of the esterified to the total cholesterol (ester quotient) in the serum is extremely constant, in the thrombocytes and leucocytes it varies widely²⁴. Various colorimetric methods have been developed for the assay of cholesterol, but none is very specific²⁵, most used are those of SCHÖNHEIMER and SPERRY²⁶, ABELL²⁷ and ZAK²⁸.

Like the total lipid content, the cholesterol content of the serum depends on various factors, with the diet and bodily activity playing a particularly important role. The serum cholesterol level is affected less by the cholesterol content of the diet - most of the serum

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Serum lipoproteins and their composition¹

Fraction	Content* (g/l serum)	Density	S _f **	-S**	Free electrophoresis (fraction)	Conn fraction (method 10)	Lipoprotein composition							
							Protein (%)	Lipids (%)	Lipid fraction as percentage of total lipids					
									Glycerides	Phosphatides	Cholesteryl esters	Free cholesterol	Nonesterified	
Chylomicrons.....	0-0.5	< 0.96	10 ⁴ -10 ⁵	-	-	I+II	1	99	88	8	3	1	-	
β-Lipoproteins, low-density	LDF ₁	1.5	0.96-1.006	20-400	>70	α ₂	I+II	7	93	56	20	15	8	1
	LDF ₂	0.5	1.006-1.019	12-20	40-70	α ₂	I+III	11	89	29	26	34	9	1
	LDF ₃	3.5	1.019-1.063	0-12***	20-40	β	III	21	79	13	28	48	10	1
α-Lipoproteins, high-density	HDL ₂	0.5	1.063-1.125	-	4-20	α ₁	IV+V	33	67	16	43	31	10	-
	HDL ₃	3.0	1.125-1.210	-	0-4	α ₁	IV+V	57	43	13	46	29	6	6
Nonesterified fatty acids-albumin ..	40.0	-	-	-	-	V	99	1	0	0	0	0	0	100

¹ OLSON and VESTER, *Physiol. Rev.*, 40, 677 (1960).
* Average post-absorptive values for a healthy, well-nourished man aged 40 years.
** S_f = SVEDBERG flotation units (-S × 10⁻¹³ s) at a density of 1.063 and t = 26°C; -S = SVEDBERG flotation units at a density of 1.21 and t = 26°C.
*** Fractions 0-2 are high-density lipoproteins (HDL₁).

Serum lipoprotein concentrations at various ages (g/l)¹

Age	Number	S _f 100-400		S _f 20-100		S _f 12-20		S _f 0-12		HDL ₁		HDL ₂		HDL ₃	
		Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s
Men															
17-29	585	0.37	0.43	0.75	0.41	0.40	0.21	3.22	0.86	0.23	0.07	0.37	0.28	2.17	0.40
30-39	834	0.51	0.64	0.91	0.54	0.51	0.23	3.55	0.84	0.24	0.15	0.36	0.28	2.19	0.42
40-49	399	0.66	0.91	1.07	0.66	0.57	0.23	3.80	0.84	0.25	0.15	0.37	0.28	2.26	0.50
50-65	143	0.58	0.70	1.03	0.58	0.56	0.24	3.83	0.75	0.27	0.22	0.42	0.32	2.24	0.51
Women															
17-29	190	0.09	0.14	0.44	0.29	0.30	0.16	2.83	0.68	0.21	0.07	0.80	0.41	2.28	0.38
30-39	99	0.13	0.17	0.51	0.36	0.41	0.22	3.24	0.86	0.22	0.09	0.81	0.45	2.35	0.39
40-49	37	0.18	0.24	0.65	0.51	0.42	0.21	3.46	0.67	0.23	0.05	0.89	0.53	2.41	0.43
50-65	10	0.32	0.37	0.77	0.48	0.93	0.36	4.37	0.40	0.25	0.07	1.17	0.66	2.70	0.54

¹ LINDGREN and NICHOLS, in PUTNAM, F. W. (Ed.), *The Plasma Proteins*, vol. 2, Academic Press, New York, 1960, page 1 (values determined in healthy employees of the University of California Radiation Laboratory, Livermore, Calif.).

Serum lipid concentrations at various ages

Serum lipid concentrations at various ages

	Num-ber	Total lipids (g/l)			Total cholesterol (g/l)			Free cholesterol (g/l)			Phospholipids (g/l)			Glycerides (g/l)			Nonesterified fatty acids (mmol/l)		Refer-ence	
		Extreme range		Mean	95% range (extreme range in brackets)		Mean	Extreme range		Mean	Extreme range		Mean	95% range		Mean				
		5%	95%		2.5%	97.5%		5%	97.5%		50%	95%		2.5%	97.5%		5%	95%		
Mothers	36	-	-	9.03	-	-	2.60	-	-	0.66	-	-	2.76	-	-	2.28	-	-	1	
Cord blood	21	-	-	2.91	-	-	0.75	-	-	0.15	-	-	0.99	-	-	0.69	-	-	1	
Children, 6-8 weeks	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	
Milk and meat diet	10	-	-	5.74	-	-	1.36	-	-	0.30	-	-	1.77	-	-	1.83	-	-	1	
Vegetable diet	10	-	-	3.83	-	-	0.89	-	-	0.17	-	-	1.32	-	-	1.10	-	-	1	
Cord blood	15	3.13	(1.70-4.40)	-	0.74	(0.48-0.98)	-	0.26	(0.19-0.38)	-	1.24	(0.76-1.70)	-	-	-	-	-	-	2	
Children, 3-10 days (breast fed)	15	6.08	(4.30-7.60)	-	1.34	(1.10-1.67)	-	0.49	(0.37-0.59)	-	2.07	(1.60-2.60)	-	-	-	-	-	-	2	
Children, 1-12 months	37	6.06	(2.40-8.00)	-	1.30	(0.69-1.73)	-	0.40	(0.27-0.66)	-	1.88	(1.22-2.76)	-	-	-	-	-	-	2	
Children, 2-14 years	25	8.38	(4.90-10.90)	-	1.88	(1.38-2.42)	-	0.54	(0.39-0.69)	-	2.35	(1.88-2.92)	-	-	-	-	-	-	2	
Children, 10-13 years	635	-	-	-	1.54	1.07-2.06	-	-	-	-	-	-	0.75	0.35-1.74	-	-	-	-	2	
Men, 16-35 years	62	6.10	-	-	1.20	1.92	-	0.57	0.64	-	0.19	2.08	-	0.35	0.84	0.34	0.750	0.233	4	
Women, 16-35 years	29	6.48	-	-	1.14	1.85	-	0.38	0.58	-	0.18	2.32	-	0.44	0.88	-	0.781	0.174	4	
Adults, 20-35 years	62	-	-	-	1.78	-	-	0.26	0.46	-	1.78	-	0.23	1.23	-	0.49	0.405	0.081	6	
Adults, 45-70 years	30	-	-	-	2.09	-	-	0.29	0.61	-	2.50	-	0.28	-	-	-	-	-	6	

	Num-ber	Total lipids* (g/l)			Total cholesterol* (g/l)			Phospholipids* (g/l)			Glycerides* (g/l)			Refer-ence	
		Extreme range		Mean	95% range (extreme range in brackets)		Mean	Extreme range		Mean	95% range		Mean		
		5%	95%		2.5%	97.5%		5%	97.5%		2.5%	97.5%		5%	95%
Men, 15-24 years	150	3.95	4.15	5.82	8.29	8.63	148	1.21	1.42	1.87	2.59	2.78	150	1.45	1.51
Men, 25-34 years	383	4.58	4.81	6.50	9.35	9.95	379	1.67	1.62	2.11	2.94	3.12	383	1.58	1.66
Men, 35-44 years	497	4.93	5.18	7.12	10.91	11.89	494	1.60	1.76	2.37	3.31	3.54	495	1.70	1.82
Men, 45-54 years	499	5.16	5.33	7.44	10.26	11.24	497	1.61	1.77	2.45	3.34	3.49	499	1.77	1.86
Men, 55-64 years	301	5.33	5.55	7.69	10.50	11.73	301	1.75	1.83	2.54	3.28	3.55	303	1.80	1.94
														2.43	3.06
														0.23	0.31
														0.98	2.49
														0.10	0.98
														0.07	0.07
														2.57	2.74
														1.93	2.15
														1.66	2.15
														1.58	1.98
														3.12	3.83
														2.76	2.98
														2.76	3.11
														2.32	3.00
														1.82	2.32
														1.70	1.88
														3.54	4.05
														3.49	4.09
														3.49	4.09
														3.09	3.21
														2.39	3.09
														1.86	2.39
														1.94	2.43
														0.23	0.31
														0.98	2.49
														0.10	0.98
														0.07	0.07
														2.57	2.74
														1.93	2.15
														1.66	2.15
														1.58	1.98
														3.12	3.83
														2.76	2.98
														2.76	3.11
														2.32	3.00
														1.82	2.32
														1.70	1.88
														3.54	4.05
														3.49	4.09
														3.49	4.09
														3.09	3.21
														2.39	3.09
														1.86	2.39
														1.94	2.43
														0.23	0.31
														0.98	2.49
														0.10	0.98
														0.07	0.07
														2.57	2.74
														1.93	2.15
														1.66	2.15
														1.58	1.98
														3.12	3.83
														2.76	2.98
														2.76	3.11
														2.32	3.00
														1.82	2.32
														1.70	1.88
														3.54	4.05
														3.49	4.09
														3.49	4.09
														3.09	3.21
														2.39	3.09
														1.86	2.39
														1.94	2.43
														0.23	0.31
														0.98	2.49
														0.10	0.98
														0.07	0.07
														2.57	2.74
														1.93	2.15
														1.66	2.15
														1.58	1.98
														3.12	3.83
														2.76	2.98
														2.76	3.11
														2.32	3.00
														1.82	2.32
														1.70	1.88
														3.54	4.05
														3.49	4.09
														3.49	4.09
														3.09	3.21
														2.39	3.09
														1.86	2.39
														1.94	2.43
														0.23	0.31
														0.98	2.49
														0.10	0.98
														0.07	0.07
														2.57	2.74
														1.93	2.15
														1.66	2.15
														1.58	1.98
														3.12	3.83
														2.76	2.98
														2.76	3.11
														2.32	3.00
														1.82	2.32
														1.70	1.88
														3.54	4.05
														3.49	4.09
														3.49	4.09

* Simple percutaneous
 † Swanson et al., *Pediatrics*, 27, 765 (1961) (maternal of a Tennessee an-
 phylax home)
 ‡ Bazzarello and Swanson, *Acta paediatrica (Uppsala)*, 43, 221 (1954), Rap-
 ersson, S., *Acta paediatrica (Uppsala)*, 44, suppl 102 (1955) (healthy chil-
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* Bazzarello, *Am J Clin Nutr*, 20, 850 (1967) (schoolchildren in New
 York City)
 † Swanson et al., *Acta med scand*, 169, 43 (1963) (healthy adults in Göte-
 borg, Sweden)

* Bazzarello, *Am J Clin Nutr*, 20, 850 (1967) (schoolchildren in New
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 York City)
 † Swanson et al., *Acta med scand*, 169, 43 (1963) (healthy adults in Göte-
 borg, Sweden)

Fatty acid composition of the serum lipid fractions of adults¹

	Non-esterified fatty acids	Cholesteryl esters	Phosphatides	Triglycerides
Lipid fraction (g/l serum)	0.29	2.24	2.09	1.73
Fatty acids of lipid fraction (g/l serum)	0.29	0.72	1.11	1.44
Fatty acids (% of total)				
Myristic acid	2.0	1.1	0.9	1.6
Palmitic acid	27.9	12.1	30.7	28.1
Palmitoleic acid	7.2	6.8	3.3	7.6
Stearic acid	14.9	2.6	11.9	3.7
Oleic acid	25.5	18.9	15.1	36.8
Linoleic acid	13.1	47.1	21.5	12.2
Triene acids (C ₁₈ and C ₂₀)	0.9	0.9	0.8	0.9
Arachidonic acid	2.4	5.0	8.8	3.1
Pentaene acids (C ₂₀ and C ₂₂)	1.2	1.4	2.0	1.2
Hexaene acids (C ₂₂)	1.8	1.9	3.1	1.9
Other	3.1	2.2	2.1	2.9

¹ SCHRADER, W., *Med. u. Ernähr.*, 1, 267 (1960); SCHRADER et al., *Klin. Wschr.*, 38, 739 (1960) (mean values from 16 healthy subjects aged 18-41 years).

For the fatty acid composition of the lipid fractions in the newborn see ZÖLLNER et al., *Klin. Wschr.*, 44, 380 (1966), in the newborn and infants in relation to diet see PRIKAAR and FERNANDES, *Amer. J. clin. Nutr.*, 19, 194 (1966).

Phosphatides in the plasma and erythrocytes¹

	Plasma (15 adults*)		Erythrocytes (13 adults)	
	Mean	s	Mean	s
Lipid phosphorus (mg/l)	99.8	15.2	139.5	11.1
Phosphatides (% of lipid phosphorus)				
Cephalin**	5.0	0.6	42.4	1.1
Lecithin	68.2	1.7	32.7	2.1
Sphingomyelin	19.0	1.9	23.1	1.1
Lysolecithin	7.7	1.5	1.8	0.4

* Fasting values. In the cord plasma the proportion of lecithin is less than that of the other fractions higher².

** In the serum³ about one-third of the cephalin fraction consists of plasmalogens, in the erythrocytes⁴ about one-half.

¹ PHILLIPS, G. B., *J. Lab. clin. Med.*, 59, 357 (1962).

² ZÖLLNER et al., *Klin. Wschr.*, 44, 380 (1966).

³ PHILLIPS, G. B., *Biochim. biophys. Acta (Amst.)*, 29, 594 (1958).

⁴ FARQUHAR, J. W., *Biochim. biophys. Acta*, 60, 80 (1962).

Suggested nomenclature of changes in the serum lipid tent¹

	Designation for an increase in the serum concentration
Cholesterol	Hypercholesterolaemia
Lipid phosphorus	Hyperphosphatidaemia
Neutral fat	Hyperlipaemia
Free fatty acids	Hyperlipidaemia
Total lipids	Hyperlipidaemia
Clouding by neutral fat	Lipaemia

¹ KLENK et al., *Clin. chim. Acta*, 7, 446 (1962).

Carbohydrates (for references see page 606)

Glucose, fasting values (mg/l)

	Determined in	Method	Number	Mean	95% range	s	Reference	Remarks
Pregnancy	Capillary blood	HAGEDORN-JENSEN	19	931	878-984	26.7	¹	<i>Methods.</i> Reduction method: determining 'blood sugar' - instance HAGEDORN-JENSEN, H. MAN, FOLIN-WU, SOMOGYI-NELSON - determine other hexoses (lucose, mannose, galactose), pentose, glucuronic acid, glutathione, acid, creatine and creatinine, corbic acid and various drug addition to glucose. Aldohexoses can be determined colorimetrically with o-toluidine ^{7,10} or triphenyl tetrazolium chloride ¹¹ . Most specific are the enzymatic methods using either glucose oxidase ¹² , peroxidase ^{8,12,13} or hexokinase ¹⁴ with glucose-6-phosphate dehydrogenase ^{1,2} .
Newborn	Cord blood	HAGEDORN-JENSEN	20	856	790-922	33.2	¹	
		Glucose oxidase	20	671	588-754	41.5	¹	
1st hour	Capillary blood	HAGEDORN-JENSEN	20	558	489-627	34.4	¹	
		Glucose oxidase	20	263	190-336	36.5	¹	
6th day	Capillary blood	HAGEDORN-JENSEN	16	708	653-763	27.5	¹	
		Glucose oxidase	16	447	381-513	32.8	¹	
Newborn	Cord blood	SOMOGYI-NELSON	14	730	392-1068	169	²	
1 hour	Capillary blood	SOMOGYI-NELSON	14	626	224-1028	201	²	
2 hours	Capillary blood	SOMOGYI-NELSON	14	589	209-969	190	²	
9 hours	Capillary blood	SOMOGYI-NELSON	14	590	310-870	140	²	
24 hours	Capillary blood	SOMOGYI-NELSON	14	579	301-857	139	²	
48 hours	Capillary blood	SOMOGYI-NELSON	14	591	321-861	135	²	
Newborn 1-78 hours	Blood	HAGEDORN-JENSEN	63	841	-	-	³	
		SOMOGYI-NELSON	63	598	-	-	³	
Children 1-17 months	Blood	HAGEDORN-JENSEN	10	948	-	-	³	
		SOMOGYI-NELSON	10	796	-	-	³	

Physiological and pathological variations. After 12 hours fasting glucose level in the capillary blood approximates to that in the venous blood; after glucose intake higher in the capillary and art than in the venous blood. In leucocytosis there may be a false appearance of hypoglycaemia owing to glycolysis in the leucocytes¹⁴. Concentration of glucose is the same in the serum water and erythrocytes.

Glucose, fasting values (mg/l) (continued)

	Determined in	Method	Number	Mean	95% range	<i>s</i>	Reference	Remarks (continued)
Children 2-14 years	Blood	HAGEDORN-JENSEN	15	933	—	—	3	water. The blood glucose level falls during the first hours of life and then rises slowly over the next few days ^{1, 2, 18} ; this hypoglycaemia of the newborn is particularly marked in premature infants ^{16, 17} , in poorly nourished children ¹⁸ and in children of diabetic mothers ¹⁴ . The blood glucose level is pathologically increased in diabetes and adrenocortical (Cushing's syndrome) or pituitary disorders (acromegaly), after administration of ACTH, by an increase in the amount of circulating adrenaline, and in Wernicke's encephalopathy, it is decreased in insulin excess, the dumping syndrome, impairment of adrenocortical (Addison's disease) or pituitary function, lesions of the hypothalamus and some liver diseases.
Adults	Blood	SOMOGYI-NELSON	15	843	—	—	3	
		HAGEDORN-JENSEN	21	1072	—	—	3	
		SOMOGYI-NELSON	21	1000	—	—	3	
Children 8-14 years	Venous blood	Glucose oxidase	12	800	600-1000	—	4	
Adults	Venous plasma	SOMOGYI-NELSON	33	995	819-1171	88	8	
		Glucose oxidase	33	909	751-1067	79	8	
Adults	Venous blood	Glucose oxidase	38	800	668-932	66	8	
Adults	Blood	α -Toluidine	21	—	630-870	—	7	
Adults	Blood	Glucose oxidase	94	810	630-990	90	8	
Birth-29 years	Capillary blood	HOFFMAN	41	859	683-1035	88	9	
30-49 years	Capillary blood	HOFFMAN	103	878	650-1106	114	9	
50-69 years	Capillary blood	HOFFMAN	155	897	623-1171	137	9	
70 years and over	Capillary blood	HOFFMAN	46	921	665-1317	163	9	
17-45 years	Capillary blood	Hexokinase	199	828	700-950	65.6	10	

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	<i>s</i>	Reference	Mean	95% range	<i>s</i>	Reference	
Pentoses (mg/l)					6.6	0.2-13.0	3.2	19	Values from 28 subjects, determined with orcinol
L-Xylulose					1.4	0-5.0	1.8	20	Values from 36 subjects. Increased in diabetes
Galactose (mg/l)	15.9	3.4-28.4	6.25	20					Values from 100 subjects, determined enzymatically.
Mesoinositol (mg/l)					10.9	6.7-15.1	2.1	21	Values from 18 subjects, determined enzymatically
Sugar phosphates (μ mol/l)									
Diphosphoglyceric acid	4420	600-8240	1910	22					
Phosphoenolpyruvic acid	8.8	3.6-14.0	2.6	22					
2-Phosphoglyceric acid	4.3	0.7-7.9	1.8	22					
3-Phosphoglyceric acid	61.2	35.4-86.0	12.4	22					
Glyceraldehyde 3-phosphate	2.6	1.2-4.0	0.7	22					
Dihydroxyacetone phosphate	4.9	0-11.9	3.5	23					
Glucose 6-phosphate	24.8	5.2-44.4	9.8	22					
Fructose 6-phosphate	5.4	3.4-7.4	1.0	22					
Fructose 1,6-diphosphate	4.6	2.6-6.6	1.0	22					
Pentose 5-phosphate	18	0-36	9	23					
Nucleotide pentose	3900	2630-4980	590	23					
Sedoheptulose 1,7-diphosphate	9	—	—	24					
Oxulose 1,8-diphosphate	3	—	—	24					
Galactose 1-phosphate (mg/l)									
Cord blood	17	1-33	8	25					Increased in galactosaemia
Children, adults	0	0-6	3	25					
Glucuronic acid, total (mg/l)									
(a) Children					65	—	—	26	Values from (b) 56, (c) 44 subjects determined with (a) carboxate, (b, c, d) naphthoresorcinol. Component of glycoproteins (see page 606), in serum occurs mainly bound to glucosides, but part is free ²⁹ . The serum glucuronic acid level is decreased in the newborn.
(b) Men					32	19.6-44.4	6.2	27	
(c) Women					32	23-41	4.5	27	
(d)		Erythrocytes (0-20)	—	28					

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Glycogen (mg/l)	55	(12-162)	-	31	0	-	-	31	In glycogen storage disease content of the erythrocyte creased ^{32,34} .
(μ g/g haemoglobin)									
Newborn, 1st day	155	Erythrocytes: (48-361)	-	32					
Children, 1-12 months	86	(32-151)	-	32					
Adults	56	(26-105)	-	32					
(mg/10 ⁹ cells)	7.5	Granulocytes: (4.7-11.9)	-	33					
Heparin (mg/l)	-	(1.0-2.4)	-	35	
Protein-bound carbohy- drates (glycoproteins) (mg/l)									
Total	2739	-	-	36	Various proteins in the seru- cytes, leucocytes and throm- bin carbohydrates ^{38,39} . Fo- hydrate content of the seru- teins see page 581. The he- serum glycoproteins are ga- mannose, the hexosamines ine and glucosamine (in the r
Hexoses	1210	1170-1250	21	36	
Hexosamines	830	750-910	40	36	
Sialic acid	600	526-674	37	36	
Fucose	89	77-101	6	36	
Uronic acids	2.3	0.8-3.8	0.75	37	

The serum level of protein-bound carbohydrates is the same in men and women⁴¹ (there is an increase towards term in pregnancy⁴²); that of sialic acid^{41,43} and hexoses^{42,44} increases with age. The serum sialic acid level in the newborn is lower than in the mother^{45,46} and attains the adult level

within 4 months⁴⁶. The serum glycoprotein level is increased in accompanied by tissue breakdown, in the collagen diseases, and in in and degenerative disorders. For further discussion of the pathology in the glycoproteins see the literature^{38,42,47}.

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Non-nitrogenous metabolites (for references see page 608)

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range	s	Refer- ence	
Ethyl alcohol (mg/l)	-	(<1.5)	-	34	For colorimetric determination SHINE et al. ³⁵ .
Acetaldehyde (mg/l)	2.3	(0.5-4.0)	-	36	Increased in alcoholic poisoning, detected in the breath when the concentration exceeds 5 mg/l.
Acetoin (mg/l)	0.10	-	-	37					

Blood - Non-nitrogenous Metabolites

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
3-Butyrene glycol (mg/l)	1.17	-	-	27					
Glycerol (mg/l)									
(a) Children, 8-14 years....	5.5	0.9-10	-	32	Values from (a) 12, (b) 15, (c) 51 jects for the free glycerol. Glycerol mainly present as a component of glycerides (see under 'Lipids', page 601)
(b) Adults	7.5	2.9-12.1	2.3	38	
(c) Adults	11	0-23	6	40	
Volatile acids (mg/l) ..	17	-	-	1	About 25% consists of formic acid, of acetic acid and 0-5% of prop- ionic acid
Fatty acids	See under 'Lipids', page 601
Malic acid (mg/l)....	4.6	(2.4-7.5)	-	2	0.43	0.19-0.67	0.12	3	Serum values from 14 subjects determined enzymatically. Increased in insufficiency
Succinic acid (mg/l)	5	-	-	4	
Citric acid (mg/l)									
Umbilical vein	16.9	4.3-29.5	6.3	6					Values (a) from 29 fasting subject creases by 4-9 mg/l after a meal
Umbilical artery	13.0	8.2-17.8	2.4	6					
Adults	-	(13.0-16.7)	-	6	-	(19.2-26.0)	-	6	
(a) Adults					26	(17-31)	-	7	
Lactic acid (mg/l)									
(a) Umbilical vein	196	60-332	68	11					Values from (a) 14, (b) 69 subjects ues (b) in arterial blood of fasting jects completely at rest, (c) in ve- blood under the usual conditions colorimetric assay see BARKER et for enzymatic methods see OLSON & BERGMAN ¹⁸
(a) Newborn, 1 hour	160	40-280	60	11					
(a) Newborn, 1 day	144	28-260	58	11					
(a) Newborn, 2 days	135	41-229	47	11					
(b) Adults	56	42.2-69.8	6.9	12					
(c) Adults	90	68.4-112	10.8	12					
	76	Erythrocytes 32-120	22	16					
The blood lactate level is increased by muscular activity and emotional excitement in the newborn (especially in the arterial cord blood) ^{11, 12} , and towards term in pregnancy ¹⁹ , often decreased in renal insufficiency ² . A syndrome associated with a high blood lactate level (lactacidosis) has been described ¹									
Oxalic acid (mg/l)	-	(2.0-3.2)	-	20	-	(1.4-2.8)	-	20	Values from 15 adults on a normal diet
Glyoxylic acid					0	-	-	20	
Pyruvic acid (mg/l)									
Umbilical vein	7.1	1.1-13.1	3.0	6					Values from (a) 120, (b) 21 subjects values (b) determined enzymatically venous blood of fasting subject complete rest. Pyruvic and other acids are unstable and should therefore be determined in whole blood rather than in serum
(a) Children, 2-13 years	6.73	4.93-8.53	0.90	21					
(b) Adults	5.6	1.2-10.0	2.2	22	6.4	2.6-10.2	1.9	22	
	8.2	Erythrocytes 2.6-13.8	2.8	13					
The blood pyruvate level is high in the newborn and falls during the first days of life ^{22, 23} . It is increased by glucose intake, muscular effort and emotional excitement. Pathological increases are seen in vitamin B ₁₂ deficiency, respiratory alkalosis, severe cardiovascular disturbances, arsenic and mercury poisoning and liver disease. For a review see NOODMAN and NOODMAN ¹⁰									
a-Ketoglutaric acid (mg/l)									
Cord blood	2	-	-	8					Values from (a) 120, (b) 40 subjects physiological and pathological changes in the blood a-ketoglutarate level much the same as those in the pyruvate level.
(a) Children, 2-13 years	1.36	0.70-2.02	0.33	21					
(b) Children, adults	1.3	0.5-2.1	0.4	24					
a-Ketoisovaleric acid (mg/l)	1.3	0.9-1.7	0.2	24					Values from 40 children and adults

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
α -Ketoisocaproic acid and α -keto- β -methylvaleric acid (mg/l)	3.8	1.8-5.8	1.0	24	Values from 40 children 21
Oxaloacetic acid (mg/l) ...	1.2	-	-	25					
Ketone bodies (μ mol/l)									
(a) Newborn, < 4 hours ...	90	(40-180)	-	26	Values (a) in capillary blood (b) from 94, (c) from 19 sub- stitution from values (b) given acetone or 14.9 mg β -hydroxy- acid per litre. Few methods mining ketone bodies are satisfactory. Acetoacetic and β -hydroxybutyric can be determined by specific methods (see values below).
(a) Newborn, 2-6 days	670	(90-1900)	-	26					
(a) Children, 1 week-1 year	250	(30-890)	-	26					
(a) Children, 1-2 years	540	(40-2300)	-	26					
(a) Children, 2-6 years	290	(30-1100)	-	26					
(a) Children, 6-15 years	130	(10-540)	-	26					
(b) Adults, fasting	143	5-281	69	27					
(c) Adults, non-fasting	107	0-247	70	27					

25-35% of the blood ketone bodies consist of acetoacetic acid and acetone, 65-75% of β -hydroxybutyric acid^{29,30}. The level is increased by long fasting. For the biochemical basis of ketone-body formation see the literature³¹.

The ketone bodies of blood are pathologically increased in untreated glycogen storage disease, alkalosis, CUSHING's syndrome and under of growth hormone.

Acetone (mg/l)									
(a) Children, 1-3 years	12	(0-37)	-	28	Values from (a) 50, (b) 47, (c) 7 subjects.
(b) Children, 10-15 years	9	(0-34)	-	28	
(c) Adults	2.9	2.3-3.5	0.3	32	
Acetoacetic acid (mg/l)*									
(a) Children, 1-3 years	6	(0-32)	-	28	Values from (a) 45, (b) 43, (c) 7 subjects; values (d, e) determined enzymatically.
(b) Children, 10-15 years	3	(0-28)	-	28	
(c) Adults	-	(0.55-2.6)	-	33	-	(0.80-2.8)	-	33	
(d) Adults, non-fasting	1.7	(0.5-4.6)	-	30					
(e) Adults, fasting	3.2	(1.8-7.8)	-	30					
β -Hydroxybutyric acid (mg/l)**									
(a) Children, 1-3 years	13	(0-35)	-	28	Values from (a) 11, (b) 17, (c) 7 subjects; values (c, d) determined enzymatically.
(b) Children, 10-15 years	9	(0-25)	-	28	
(c) Adults, non-fasting	3.7	(1.4-9.9)	-	30					
(d) Adults, fasting	9.4	(5.8-17.1)	-	30					
Lipoic acid (μ g/l)	15.8	8.8-22.8	3.5	41	Values from 10 subjects.

* 1 mg/l = 9.8 μ mol/l. ** 1 mg/l = 9.6 μ mol/l.

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Blood - Vitamins

(For references see page 613)

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Reference	Mean	95% range (extreme range in brackets)	s	Reference	
Carotenes (μg/l)	850	(200-1990)	-	7	Values from 133 adults on a normal carotene content
The serum carotene level is rather high towards term in pregnancy ² ; in cord blood it is about 25% of that in the maternal blood ² . In infants it is often					increased, probably as a result of the high intake of milk and vegetables; for children are within the above normal range ⁴				
Vitamin A (μg/l)	324	(207-471)	-	7	Values from 133 adults on a normal carotene and vitamin content
In the serum about 90% of the vitamin A is present as alcohol, the rest as ester, almost all is bound to the plasma proteins (see page 457). So the body's reserve of the vitamin are not exhausted, the serum level is constant. It is pathologically decreased in infections, in lobular pneumonia it may disappear completely from the serum ⁸									
Vitamin D (IU/l)									
Children	-	(800-2100)	-	7 ⁹	Values by biological method (see page 457)
Adults	2000	(700-3100)	-	7	In the serum, vitamin D is bound to globulins and albumin (see page 457)
Tocopherol (mg/l)									
(a) Cord blood	5.7	(1.0-11.2)	-	9	Values from (a) 46, (b) 71, (c) 100 by (d) method of Na Macao ¹⁰ and (b), c) method of et al. ¹¹
(b) Men	10.6	5.6-15.6	2.5	9	
(c) Women	10.4	5.0-15.8	2.7	9	
The serum tocopherol is 85% α, the remainder β and γ-tocopherol ¹² . The serum level is increased in pregnancy ¹³ , it is decreased in the newborn and various tocopherol-deficiency states, particularly cystic pancreatic fibrosis (see page 466) ¹⁴ . Breast fed infants have higher serum levels than those on milk ¹⁵									
Ubiquinone (mg/l)					0.73	(0.40-1.15)	-	10	The serum contains ubiquinone
Thiamine (μg/l)									
(a) Total	23	(20-75)	-	17	21	(18-62)	-	17	Values (a) from 138 (whole blood 123 serum) subjects determined by the method of J. H. J. van der Meer, values (b) from subjects determined by <i>Ochromococcus ananias</i> , values (c) from 11 subjects by the method of Total thiamine determined after hydrolysis of aminopyrophosphate
(b) Total	-	(20-41)	-	10	-	(3-15)	-	18	
(c) Total	-	(10-70)	-	18	-	-	-	-	
(c) Free	-	(6.5-11.4)	-	10	-	-	-	-	
The thiamine of the erythrocytes and leucocytes is mainly pyrophosphate (see page 470). The serum thiamine level is lower towards term in pregnancy (mean 11.5 μg/l), higher in the newborn (mean 55 μg/l) ²⁰ . The fall in the erythrocyte thiamine pyrophosphate level in thiamine deficiency is of diagnostic value in the transketolase test (see page 470). The blood level is low in insulin dependent diabetes ²¹ .									
Riboflavin (μg/l)									
(a) Total	66.8	(49-104)	-	22	-	-	-	-	Values (a) from 18 men and 42 by the lumiflavin method, values from 13, (c, d) from 12 subjects photometrically, values (b) from 8 subjects by using <i>Lactobacillus</i>
(a) As FMN and FAD	55.1	(43-71)	-	22	-	-	-	-	In cord blood serum the level of riboflavin is 4 times that of FMN that of FAD half, as high as in the normal serum ²² . A lowered erythrocyte riboflavin level indicates riboflavin deficiency ²³ (see page 473)
(b) Total	-	-	-	-	32	(26-37)	-	23	
(b) As FAD	-	-	-	-	24	(18-30)	-	23	
(b) Free and as FMN	-	-	-	-	8	(3-13)	-	23	
(c)	224	Erythrocytes (180-262)	-	23	-	-	-	-	
(d)	2520	Leucocytes (2270-2930)	-	23	-	-	-	-	
(e) (μg/10 ⁶ cells)	0.62	0.18-1.06	0.22	24	-	-	-	-	
Vitamin B ₆									
Total activity (μg/l)									
(a)	37	(20-45)	-	27	44	(30-80)	-	27	Values determined by means of <i>Salmonella pyroformis</i> , (b, c) <i>Saccharomyces cerevisiae</i> , values from (b) 30 subjects
(b) Men	19.2	(6.8-77)	-	28	-	-	-	-	For methods of determining see the literature ^{27, 28} and page
(c) Women	17.7	(4.4-76)	-	28	-	-	-	-	
(d)	20	Erythrocytes (13-31)	-	27	-	-	-	-	

The vitamin B₆ activity of the blood is probably mainly due to pyridoxal phosphate. pyridoxal appears to be absent²¹. The blood level is rather low during

pregnancy^{21, 22}, in the cord blood the concentration is about 4 times the maternal blood²²

Blood - Vitamins

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Pyridoxal phosphate ($\mu\text{g/l}$)									
(a) Birth-1 year	16.3	(6.5-57.1)	16.7	33	Values from (a) 14, (b) 13, (c) 11, (e) 40 subjects by the tyrosine decarboxylase method.
(b) 20-29 years	11.3	(3.8-21.6)	5.7	33	
(c) 30-59 years	7.1	(2.4-12.4)	3.0	33	
(d) 60 years and over	3.4	(0-13.5)	3.0	33	
(c) ($\mu\text{g}/10^9$ cells)	-	Leucocytes: (0.14-0.36)	-	34					
Pyridoxic acid ($\mu\text{g/l}$)	-	(100-130)	-	31	Values from 3 subjects determined rometrically.
Nicotinic acid (mg/l)									
(a)	-	(3.9-9.6)	-	29	-	(0.016-0.05)	-	29	Values from (a) 28, (b) 39, (c) 46 jects by means of (a) <i>Tetrahymena</i> <i>formis</i> , (b, c) <i>Lactobacillus arabinosus</i> . In whole blood the nicotinic acid or almost exclusively as nicotinamide nucleotides (NAD and NADP) in cells (in the erythrocytes 60-90 mg, the leucocytes 88 mg/l, expressed NAD ³⁶).
(b) Men	6.55	5.32-7.78	0.615	35					
(c) Women	6.05	4.59-7.51	0.730	35					
1-Methylnicotinamide (mg/l)	0.017	-	-	36	After ingestion of nicotinamide the tabolites 1-methyl-2-pyridone-5-carb- ylamide and 1-methyl-4-pyridone-5- boxylamide are found in the plasma
Vitamin B ₁₂ (ng/l)									
(a)	611	277-945	167	38	Values from (a) 39, (b) 223, (c) 28, 3, (e) 50 subjects determined by us (a) isotope dilution, (b) <i>Escherichia coli</i> (c, d) <i>Ochromonas rualhaverensis</i> , (e) <i>La-</i> <i>batillus leithmannii</i> . For discussion methods see the literature ^{29,43} .
(b)	356	(100-900)	-	39	
(c)	-	(120-450)	-	18	-	(140-640)	-	18	
(d)	74	Erythrocytes: (59-88)	-	40					
(e)	213	(110-500)	-	41					
(ng/kg)	-	Leucocytes: (500-4300)	-	42					
(ng/ 10^9 cells)	-	(2.45-6.65)	-	42					

About 80% of the vitamin B₁₂ of the serum is not utilizable by micro-organisms unless it is first liberated by heating. This part is bound to α_1 - and α_2 -globulins⁴⁴. Most of the vitamin B₁₂ activity of the serum appears to be due to methylcobalamin⁴⁵. The serum values show a lognormal distribution⁴⁶. The serum level is rather low during pregnancy^{47, 48}; in the cord blood it is higher than in the maternal blood⁴⁹.

The serum level is pathologically decreased in pernicious anaemia, cancer of the stomach, gastric resection, lesions of the small intestine (malabsorption syndrome), fish-tapeworm carriers and alimentary vitamin B₁₂ deficiency (example in vegetarians); it is increased in liver and renal diseases, diabetes and leukaemia^{39, 43, 45}. Serum values below 100 ng/l are indicative of severe deficiency of the vitamin (megaloblastic anaemia).

Folic acid ($\mu\text{g/l}$)									
(a)	12.0	(3.0-20.0)	-	50	Values from (a-c) 43, (d) 27, (e) 24 jects determined by means of (a) <i>Streptococcus faecalis</i> , (b) <i>Pedococcus cerevisiae</i> , (c-e) <i>Lactobacillus casei</i> . Only with the latter can 5-methyltetrahydropteroyl glutamic acid, the most important member of the folic acid group in blood, be determined (see page 478). For methods of determination see the literature ^{29, 50} .
(b)	6.35	(1.5-25.0)	-	50					
(c)	89	(47-149)	-	50	8.2	(3.5-15.0)	-	50	
(d)	327	Erythrocytes: (184-655)	-	51	9.4	(5.2-23.8)	-	51	
(ng/ 10^9 cells)									
(e)	2.6	-	1.8	52					
(c)	64	Leucocytes: -	42.5	52					

Of the serum folic acid 64% is protein-bound⁵⁴. During pregnancy the serum level is often low^{47, 50}; in the cord blood it is higher than in the maternal blood⁵⁵, but falls during the first weeks of life⁵⁶. It is pathologically decreased in diseases of the small intestine, chronic polyarthritis, myelofibrosis, carcinomatosis and dietary deficiency of the vitamin;

values below 3 $\mu\text{g/l}$ indicate severe folic acid deficiency (megaloblastic anaemia)^{50, 51}. The folic acid content of the leucocytes is increased in myeloid leukaemia⁵². The concentration in the erythrocytes and whole blood is an indication of the amount of the vitamin stored by the body⁵⁰.

Unconjugated pterins ($\mu\text{g/l}$)	-	(27-70)	-	18	-	(11-43)	-	18	Determined by means of <i>Crotalaria</i> <i>sinensis</i> .
		Erythrocytes:							

	Whole blood				Plasma or serum				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Biotin (ng/l)									
(a) Infants	324	(147-555)	114	71	Values from (a) 30, (b) 25, (c) 12 subjects by means of (a,b) <i>Lactobacillus plantarum</i> , (c) <i>Oryzomonas dozieri</i>
(b) Adults	258	(120-422)	74	71					
(c)	-	170-279	-	28	-	213-404	-	28	
Pantothenic acid (μg/l)									
(a) Total	-	(230-2075)	-	18	-	(200-1650)	-	18	Values from (a) 28, (b) 30 subjects means of <i>Lactobacillus plantarum</i>
(b) Total	464	382-546	41	18					
(b) Free	28.7	0-58.7	15	18					

During pregnancy the blood level lies within the above normal range^{20, 21}, in the newborn the level is about 5 times higher than in the maternal blood²⁰

The blood level is increased - with reduction of the liver content - in fatty acute cirrhotic livers²¹, decreased in rheumatoid arthritis²²

Ascorbic acid (mg/l)									
(a) Men, 20-30 years	5.07	(2.24-8.80)	-	63	4.76	(1.96-8.76)	-	63	Values from (a) 11, (b) 7, (c) 558, (d): (e) 50 subjects, values (a-c) determined with 2,4-dinitrophenylhydrazine. Methods see Row et al. ²³
(b) Women, 20-30 years	8.84	(5.17-12.8)	-	63	8.97	(6.24-14.1)	-	63	
(c) Children, 10-13 years					6	0-15	-	72	
(μg/10 ⁶ cells)		Leucocytes							
(d) 18-45 years	350	210-530	-	64					
(e) 60-91 years	134	20-360	-	64					

in women this proportion fluctuates during the menstrual cycle⁶⁴. Administration of corticosteroids causes dehydroascorbic acid to disappear from serum⁶⁵

Erythroblasts are all nucleated precursors of the erythrocytes; the term includes the pro-erythroblasts, the erythroblasts proper and the normoblasts. Under physiological conditions the peripheral blood contains only the last-named – and only during the first two days of life. The normoblasts closely resemble the erythrocytes in respect of plasma-staining, haemoglobin content and size. The erythroblasts proper are polychromatic in plasma-staining, the pro-erythroblasts basophile.

By erythroblastosis is understood the entry of erythroblasts into the peripheral blood; it is always a sign of increased erythropoiesis and is therefore usually accompanied by reticulocytosis. In the new-

born (including premature babies and young infants) they indicate indication of persistence or recurrence of extramedullary blood formation and at the same time of an abnormal relationship between the intensive erythrocyte formation on the one hand and the late and relatively small bone-marrow volume at this age on the other. Severe erythroblastosis of 50–100–500 or more erythro per 100 leucocytes in the early days of life is almost always a sign of severe haemolysis due to blood-group incompatibility between mother and child. In later infancy and childhood the main causes of peripheral erythroblastosis are haemolytic anaemia, haemorrhagic anaemia, and occasionally leucosis or cyanotic heart defects.

	Mean	Extreme range	s	Reference	Remarks
Number (per 100 leucocytes)					
Cord blood	3.2	(0–30)	–	1	Method: Counting in GIEMSA-stained blood smears.
Newborn, 1–10 hours	1.6	(0–16)	–	1	
Newborn, 2 days	–	(0–1)	–	1	
Adults	0	–	–	1	

Reference 1 V. HOROVICZENY and BALLÓ, *Wien.Z. inn. Med.*, 38, 196 (1957).

Reticulocytes

Synonyms: Vital-granulated erythrocytes, vital-staining erythrocytes, pro-erythrocytes (UNDRITZ¹), polychromatic erythrocytes.

The reticulocytes are erythrocytes of more than average size and more resistant to haemolysis. There is a sex difference in the reticulocyte count of 3–5 per thousand (see table below). The number of reticulocytes increases with any increase in erythrocyte formation, i.e., continuously in chronic haemolytic or haemorrhagic anaemia, suddenly and persistently for days or weeks in the reparative phase of pernicious anaemia and erythroblastopenia, to a lesser extent also in iron-deficiency anaemia. The number of reticulocytes decreases

in aplastic and hypoplastic anaemia, after transfusions and after long-continued administration of oxygen. The extent to which reticulocytes are released from the bone marrow is in general a measure of the extent of erythrocyte formation.

The wide fluctuations in the data given in the table below for normal reticulocyte counts are due to differences in the methods of measurement. The better the method of staining, the higher the reticulocyte count obtained (as in counts in smears stained with brilliant cresol blue).

	Mean	95% range (extreme range in brackets)	s	Reference	Remarks
Number					
(per μ l)	–	10 000–50 000	–	2	Values for adults by direct measurement. For newborn values see below.
(per 10 ³ erythrocytes)	7.5	1.3–13.7	3.1	3	Values for adults. For newborn values see below, for values in children and other adult values see the opposite page. (Values for children in agreement with WASHBURN ⁴ .)
Diameter (μ m)	–	(8.0–9.0)	–	5	1.0–1.5 μ m greater than that of erythrocytes (\approx 1.1–1.2 times erythrocyte diameter).
Thickness (μ m)	–	(4.5–5.5)	–	6	Erythrocytes 1.8–2.2 μ m.
Volume (μ l \approx μ m ³)					
Infants	–	(200–230)	–	6	Erythrocytes 5 μ m ³ .
Adults	–	(250–310)	–	6	Erythrocytes 85 μ m ³ .

Reticulocyte count during 1st day of life⁷

Hours	Per 10 ³ erythrocytes	Per μ l
At birth	25.4	126 000
2	35.9	168 000
4	40.0	190 000
6	26.6	148 000
8	25.1	119 000

Reticulocyte count in newborn (values per 10³ erythrocytes)

Days	FANÉN ⁸	SEIP ¹³	GAIRDNER et al. ¹²
1	22	52	37
2	20.4	50	–
3	16.6	52	–
4	10.7	45	27.5
5	5.3	33	–
6	4.8	18	–
7	3.8	13	7.9

Reticulocyte count in childhood (per 10^3 erythrocytes^{2,3})

Age	Mean	95% range	<i>s</i>
1-24 hours	39.2	-	-
1-7 days	22.3	-	-
7-10 days	10.6	-	-
10-30 days	7.9	0.3-15.5	3.8
1-2 months	12.9	0-27.7	7.4
2-6 months	10.6	0-24.8	7.1
6-12 months	7.5	0-17.3	4.9
1 year	7.5	0-16.3	4.4
2 years	7.1	0-15.1	4.0
3 years	7.2	0-15.4	4.1
4 years	8.1	0-18.1	5.0
5 years	8.2	0-17.2	4.5
6 years	7.5	0-15.5	4.0
7 years	7.6	0.6-14.6	3.5
8 years	6.8	0.4-13.2	3.2
9 years	7.5	0.9-14.1	3.3
10 years	7.6	1.2-14.0	3.2
11-15 years	7.4	0-15.4	4.0

Reticulocyte count in adults (values per 10^3 erythrocytes)

	SEIP ²		WATSON ³	
	Mean	Extrema range	Mean	95% range
Men and women ..	15.7	9.6-23.8	7.5	1.3-13.7
Men	13.5	9.6-18.4	6	1.6-10.4
Women	17.3	10.4-23.8	9	2.6-15.4

Maturity of reticulocytes (per 10^3 erythrocytes)

Degree	SEIP ²		NIZZY ^{1,2}	
	Mean	Extrema range	Mean	Extrema range ²
I	0.02	0-0.2	0	-
II	1.1	0-2.6	1.6	0-5.6
III	5.0	1.8-10.8	3.6	0.2-12.3
IV	9.5	5.8-12.0	12.5	-

References

- 1 UNDAUER, E., *Dietsch und Wöhrle*, 43, 1486 (1937)
- 2 BORMANN, S. E., *At Congrès de la Société européenne d'hématologie*, Strasbourg, 1965, page 223
- 3 WATSON, C. J., *Arch intern Med*, 86, 797 (1950)
- 4 WASHBURN, A. H., *Amer J Dis Child*, 42, 530 (1941)
- 5 PRATON, E. L., *J Clin Invest*, 7, 615 (1929)

Erythrocytes

(For other physical and chemical data see under 'Blood', pages 557-611, for references see page 616)

	Mean	95% range	<i>s</i>	References	Remarks
Erythrocyte count (red blood count, RBC)					See text below and table, page 617
Haematocrit value (lit) (packed cell volume, PCV)					See text, page 614, and table, page 617
Diameter (μm)					
(a)	8.56	8.14-8.98	0.21	1	Microscopic measurements on erythrocytes of 10 persons: (a) individual wet preparations, (b) dry preparations, (c) rouleaux. See text, page 614, and table, page 617
(b)	7.11	6.31-7.91	0.40	1	
(c)	8.70	8.12-9.28	0.29	1	
Thickness (μm)					
(a)	1.9	1.75-2.1	-	2	(a) and (b) calculated from the single cell volume and the cell diameter, (a) wet preparations, (b) dry preparations, (c) microscopic measurements on 10 persons. See also text, page 616
(b)	2.1	1.9-2.3	-	2	
(c)	1.64	1.50-1.78	0.07	1	
Surface area (μm^2)	145.0	128-162	8.3	1	Calculated from the cell diameter and cell thickness. The total surface area of the erythrocytes of an average man is ca. 3820 m^2 or some 2000 times the body surface area
	163	-	-	2	
Volume ($\text{fl} = \mu\text{m}^3$)	86.1	73.5-98.7	6.3	1	Calculated from the cell diameter and cell thickness. See text, pages 614-61 and table, page 617
Weight (μg)	96.8	-	7.02	4	Values have lognormal distribution
Haemoglobin (Hb) content					See text, page 613, and table, page 617

Erythrocyte count

Methods

The visual counting methods still used in most laboratories are subject to considerable error, the coefficient of variation in the results given by different methods being 10-15%. Automatic counting apparatus is more precise, though this applies properly

speaking only to the action of counting. The errors associated with

Counts made with the aid of ^{32}P -tagged erythrocytes have given considerably lower figures for the total numbers of circulating erythrocytes than calculations from the concentration in the peripheral venous blood. The erythrocyte concentration of the peripheral blood therefore represents an absolute value of practical diagnostic use only when the total blood volume is measured at the same time. This is shown clearly for example in the first hours of life, when the erythrocyte count often rises to over one million per microlitre while the total blood volume is reduced.

For details of the various methods of counting see the literature⁶.

Physiological characteristics

In the newborn the erythrocyte count fluctuates to a greater extent than at any other time of life, even under constant sampling conditions. It is also dependent on the site from which blood is drawn. During the first days of life the capillary blood has up to half-a-million more erythrocytes than the cord or venous blood⁷. The time at which the cord is clamped has an effect on the count. Immediate clamping prevents the passage of a quarter to one-third of the total blood volume available to the newborn child in the placenta. For this reason the erythrocyte count after a few hours in such children may lie about $1\text{--}1\frac{1}{2}$ million per microlitre below the normal level. In the newborn the erythrocyte count rises to a maximum after a few hours since the initially high blood volume is reduced by the passage of blood plasma into the tissues⁸. The erythrocyte count falls steadily from the middle of the first week of life up to the middle of the third month owing to the gradual slowing-down of erythropoiesis. The physiological polyglobulinaemia of the newborn is followed by physiological oligoglobulinaemia in the 3-month child.

During pregnancy the erythrocyte count falls⁹. In general the erythrocyte count is dependent on the partial oxygen pressure of the atmosphere and therefore on the altitude. Thus the Indians of the uplands of Peru show marked polyglobulinaemia, beginning in childhood. A very considerable increase in altitude is thus equivalent to an anoxic stimulus to erythropoiesis, descent from a high altitude (like administration of oxygen) to an inhibition. Emotional effects like anxiety and excitement can result in 'stress erythrocytosis', probably as a result of the movement of plasma into the tissues.

During puberty a sex difference in the erythrocyte count of about half-a-million develops.

Haematocrit value

The haematocrit value is the proportion of the volume of the peripheral venous or capillary whole blood occupied by the erythrocytes. On the body haematocrit see page 554. The haematocrit value is dependent on three factors, namely the erythrocyte count, the mean corpuscular volume (see below) and the plasma volume. Since the ratio between the mean corpuscular haemoglobin (see the opposite page) and the mean corpuscular volume varies between only narrow limits, the haematocrit value has almost the same significance as the haemoglobin content of the whole blood.

Measurement

The haematocrit can be measured by a variety of macro- and micro-methods. The best methods are those using high-speed haematocrit centrifuges and microhaematocrit capillaries¹⁰. The haematocrit value depends on the speed of the centrifuge, the time of centrifuging and the viscosity of the blood. The amount of plasma trapped between the packed erythrocytes is 1-9%, depending on the method¹¹; the proportion after centrifuging at $14\,000\,g$ for 40 minutes is only 0.45%¹².

See also the literature on haematocrit measurement¹³.

Physiological characteristics

By its nature the haematocrit varies in a manner similar to the erythrocyte count in newborn children; thus it is dependent on the time the cord is clamped¹⁴, rises during the first hours of life and falls up to the third month. From this time onwards, however, it behaves differently to the erythrocyte count. Whereas the latter remains more or less constant or rises slightly, the haematocrit falls somewhat because the newly-formed erythrocytes are low in haemoglobin and therefore smaller in volume. The haematocrit also resembles the erythrocyte count in respect of sex difference, behaviour during pregnancy and dependence on partial oxygen pressure of the atmosphere.

Erythrocyte diameter

Measurement

Two basically different methods are used to measure the erythrocyte diameter, micrometry and halometry¹⁵. The latter method is simple, time-saving and adequate for routine use. Measurement on blood smears or on optical projections of smears has advantage that the distribution as well as the mean value is obtained as in blood-volume measurements the former may be of diagnostic importance. Distribution values, however, should be based on measurements on at least 1500-2000 cells¹⁶.

On methods of measurement see also the literature¹⁷.

Physiological characteristics

In the newborn the erythrocyte diameter is likewise high, the unlike the erythrocyte count it continues to fall not only up to third month of life but, as a result of the formation of new erythrocytes low in haemoglobin, up to the end of the first year. The value may fall to a mean value of less than $7\,\mu\text{m}$.

Pathological characteristics

In pernicious and similar anaemias the erythrocyte diameter is high and shows a particularly wide variance. It is fairly high in aplastic anaemia, low in iron-deficiency and sideroachrestic anaemias and spherocytosis; in the latter condition a particularly important characteristic is the normal erythrocyte volume.

Numerical eccentricity

Deviation of the shape of the erythrocytes from the truly spherical is expressed as either the axis coefficient K or the numerical eccentricity ϵ as follows:

$$K = 1 - \frac{b}{a}; \quad \epsilon = \sqrt{1 - \left(\frac{b}{a}\right)^2}$$

where a = the larger, b = the smaller diameter. For the determination of these values by nomogram see v. BOROVICZÉNYI¹⁸. Normal 74.4% of the erythrocytes are spherical, 14.9% non-spherical, 8.2% elliptical and 2.5% grossly elliptical.

Predominance of regularly oval forms is known as elliptocytosis and is a dominant inheritable anomaly of no clinical significance in which all erythrocytes are similar in appearance. Symptomatic elliptocytosis of varying morphological and numerical degrees of severity occurs, usually associated with poikilocytosis, in pernicious and similar anaemias, occasionally in leukaemia and rarely in severe infections.

Morphological variations

Poikilocytes are erythrocytes of irregular shape and have an extremely wide range of size. Usually they indicate a disturbance of erythropoiesis and are probably formed by the extrusion of mass of erythroblastic or normoblastic plasma.

Round cells (spherocytes), basket cells, target cells and sickle cells are mostly phenotypic manifestations of haemolytic anaemia due to metabolic disturbances.

Erythrocyte thickness

The thickness of an erythrocyte is an arbitrary dimension since the erythrocyte is not a true rotation ellipsoid but a disk with bilateral indentations. It is of significance only when showing extreme deviations, namely in spherocytosis of hereditary origin and in phenocopy. During haemolysis the thickness increases to $4\text{--}5\,\mu\text{m}$ while the volume remains constant; this results in a lowering of the osmotic resistance of the cell. In iron-deficiency and sideroachrestic anaemias the thickness of the erythrocytes is less than $1.5\,\mu\text{m}$, so that there is an increase in the osmotic resistance.

Measurement

By direct microscopic measurement or calculation from the erythrocyte volume (mean corpuscular volume) by dividing by the square of the radius $\times \pi$.

Mean corpuscular volume (MCV)

In contrast to the erythrocyte count and haematocrit, which are dependent on various factors, the mean corpuscular volume is an absolute quantity, i.e., it has an individual though almost constant

(For other physical and chemical data see under 'Blood', pages 557-611, for references see page 616)

Measured values are of course mean values and like other biological data exhibit variance. With the aid of modern automatic erythrocyte counting instruments it is possible to obtain distribution curves of the mean corpuscular volume. In the diagnosis of anaemia such curves are capable of giving even more information than the mean corpuscular volume. Thus in aplastic, hypoplastic and especially pernicious and similar anaemias the mean corpuscular volume is high, whereas in iron-deficiency and leucoerythroblastic anaemias it is low. A high mean corpuscular volume can be simulated by a high reticulocyte count since the mean reticulocyte volume is three times greater than the mean corpuscular volume. Macrocytic haemolytic anaemia usually consists of normocytic anaemia accompanied by reticulocytosis. The high mean corpuscular volume of the newborn is also partly a result of the relatively high reticulocyte count.

Measurement

The mean corpuscular volume is calculated by dividing the haematocrit value (in litres per litre) by the number of erythrocytes in 1 litre of whole blood. The normal range so calculated is 80-90 fl (80-90 μm^3).

Mean corpuscular haemoglobin concentration (MCHC)

Under pathological conditions there is little variation, so that true diminutions of concentration by 30%, such as are found in extreme iron deficiency, are of considerable diagnostic significance.

Measurement

The mean corpuscular haemoglobin concentration (in grammes per litre erythrocytes) is calculated by dividing the haemoglobin concentration of the whole blood (in grammes per litre) by the haematocrit value (in litres per litre).

The sole physiological characteristic is the fairly high value at birth, this falls to normal by the end of the first month of life.

Mean corpuscular haemoglobin (MCH, Hb_r)

Like the mean corpuscular volume, the mean corpuscular haemoglobin (mean haemoglobin content of a single erythrocyte) is a test of iron deficiency. A value below 30 pg is known as hypochromia and is characteristic of iron deficiency and sideroblastic anaemias.

Measurement

The mean corpuscular haemoglobin is calculated by dividing the haemoglobin concentration of the whole blood (in grammes per litre) by the number of erythrocytes in 1 litre. The normal value is 30-32 pg (pg = 10^{-12} g).

Physiological characteristics

The mean corpuscular haemoglobin is likewise high in the newborn and undergoes no change during the first day of life. It then falls to normal by the third month and to moderately hypochromic values by the sixth month.

The colour index must be corrected by several factors if it is to give the same information as the mean corpuscular haemoglobin.

Haemoglobin content of the whole blood

The haemoglobin content of the whole blood is the mean corpuscular haemoglobin multiplied by the number of erythrocytes in the volume unit used. For this reason it rises and falls both with the erythrocyte count and the mean corpuscular haemoglobin.

Measurement

The recommended standard method is that of photometry.

Physiological characteristics

The haemoglobin content is subject to much the same variation as the erythrocyte count (pages 613-614) and haematocrit value (614), particularly the latter. Thus cord blood contains about 16 g/100 ml of venous blood on the first day of life about 182 g/l and capillary blood about 150 g/l.

Poverty

During pregnancy the haemoglobin content falls to a minimum of 120 g/l in the 30th-35th weeks. Lowered and increased oxygen pressures cause respectively an increase and decrease in haemoglobin content, which in this respect behaves like the erythrocyte count.

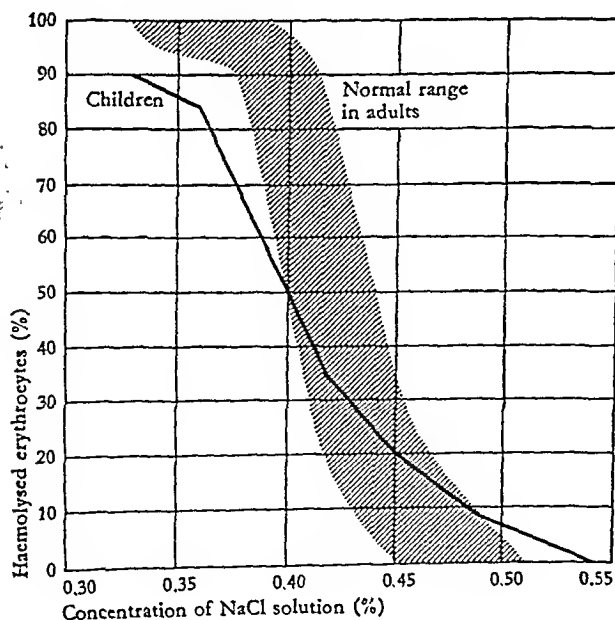
Since the haemoglobin content of the blood is a function of the erythrocyte count and the mean corpuscular haemoglobin, it is also a function of the erythrocyte count and the mean corpuscular haemoglobin.

Fetal haemoglobin

The blood of the very early foetus contains a high proportion of fetal haemoglobin, which is a dimeric protein consisting of two α -globin chains and two γ -globin chains.

(For other physical and chemical data see under 'Blood', pages 557-611)

	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Remarks
Lifetime (days)					
(a) Premature infants	—	(70-90)	—	27	Measurement: (a) and (b) by ASHBY's differential agglutination method and (d) with ¹⁵ N-glycine. The best method is that using ³² P-di-isopropyl fluorophosphate; for details of methods see the literature ^{29, 30} . A lifetime of 120 days corresponds to an erythrocyte turnover of 0.83% per day. Pathological changes in the lifetime are exclusively reductions ²⁹ .
(b) Adults	117	(110-135)	—	5	
(c) Men	120	—	—	28	
(d) Women	109	—	—	28	
Half-life (days)					
Premature infants	16	—	—	27	Measured by means of ⁵¹ Cr-tagged erythrocytes. In adults the half-life amounts to about a quarter of the mean lifetime.
Newborn	24	—	—	27	
Infants, 3 months	28	—	—	27	
Adults	29	(25-40)	—	29	
Osmotic resistance (concentration [%] of the NaCl solution used)					
(a) Cord blood					Measured on (a) 16, (b) 14 and (c) 18 subjects. For details of methods see literature ^{5, 32} ; the results are affected by the temperature, nature of the coagulant used, pH value of the haemolysing solution and bilirubin content of the blood. Complete haemolysis of the erythrocytes occurs in 0.33-0.3 NaCl solution (see diagram below). The more nearly spherical the erythrocytes, the lower the osmotic resistance ^{5, 32, 33} . Spherocytes are therefore more readily haemolysed, whereas the thinner erythrocytes are more resistant. Young mature erythrocytes are more resistant in hypotonic media than are erythrocytes ³⁴ . Erythrocytes from venous blood have a lower resistance than those from arterial blood ³⁵ . Pathological changes ^{5, 32} . Markedly reduced in congenital haemolytic jaundice and occasionally in haemolytic jaundice due to the presence of abnormal antibodies ³⁶ , increased in polycythaemia vera, thalassaemia major (resistance increased up to a NaCl concentration of 0.03%) and in sickle-cell and hypochromic anaemias.
5% haemolysis	0.502	0.46-0.55	0.022	31	
50% haemolysis	0.422	0.38-0.46	0.021	31	
(b) Newborn, 2-5 days					
5% haemolysis	0.474	0.34-0.51	0.019	31	
50% haemolysis	0.395	0.36-0.43	0.016	31	
(c) Adults					
5% haemolysis	0.475	0.45-0.50	0.012	31	
50% haemolysis	0.424	0.40-0.44	0.010	31	
Metabolism (μmol per 10^{11} erythrocytes)					
O ₂ uptake per hour	2.7	0-5.5	1.4	37	
CO ₂ formation per hour	2.5	0.3-4.7	1.1	37	
Pyruvate formation per hour ..	1.9	1.1-2.7	0.4	37	
Lactate formation per hour ..	38.4	26.6-50.2	5.9	37	

Osmotic resistance of erythrocytes³⁵

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	Mean	95% range	s	Refer- ence	Remarks																					
Leucocyte count (white blood count, WBC)	See text below and table opposite.																					
Leucocytoerit (ml/l) (leucocyte packing volume)	~2.5	Proportion of volume of the whole blood occupied by the leucocytes; culated from the leucocyte count and mean leucocyte volume.																					
Diameter.....	<table><tr><td></td><td>Diameter¹ (μm)</td><td>Volume² (μm³ [≡ fl])</td></tr><tr><td>Neutrophils</td><td>10-15</td><td>450</td></tr><tr><td>Eosinophils</td><td>10-15</td><td>450</td></tr><tr><td>Basophils</td><td>10-15</td><td>450</td></tr><tr><td>Lymphocytes</td><td>7-18</td><td>230</td></tr><tr><td>Monocytes</td><td>12-20</td><td>470</td></tr><tr><td>Neutrophil myelocytes</td><td>12-18</td><td>-</td></tr></table>		Diameter ¹ (μm)	Volume ² (μm ³ [≡ fl])	Neutrophils	10-15	450	Eosinophils	10-15	450	Basophils	10-15	450	Lymphocytes	7-18	230	Monocytes	12-20	470	Neutrophil myelocytes	12-18	-
	Diameter ¹ (μm)	Volume ² (μm ³ [≡ fl])																								
Neutrophils	10-15	450																								
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Basophils	10-15	450																								
Lymphocytes	7-18	230																								
Monocytes	12-20	470																								
Neutrophil myelocytes	12-18	-																								
Volume.....																						
Half-life (hours)																										
Granulocytes.....	6.6	3.8-9.4	1.4	3	Measured on 45 men by the ³² P-di-isopropyl fluorophosphate (DFP) method.																					
Osmotic resistance.....	After 6 minutes' exposure to 0.2% NaCl solution 55-75% of the leucocytes remain unchanged ⁴ ; mononuclear cells are less resistant than granulocytes. The resistance increases with age. It is increased in inflammatory leucocytosis as a result of the increased number of young cells and in most forms of myeloid decreased in leucopenia and pancytopenia.																					
Metabolism (mmol/10 ¹¹ leucocytes)																										
O ₂ uptake per hour.....	4.0	-	-	5	Values depend on the composition of the incubation medium.																					
Glucose consumption per hour	14.0	-	-	5																						
Lactate formation per hour..	30.1	-	-	5																						

Leucocyte count (see also the table opposite)

Measurement

Visual counting in a counting chamber or automatically using blood-cell counting apparatus. In respect of the range of error and counting differences the remarks on pages 613-614 on erythrocyte counting also apply. For discussion of methods and bibliography see the literature².

Physiological characteristics

Like the erythrocyte count the leucocyte count in the newborn is by one-fifth to one-quarter during the first hours of life (see diagram). As with the erythrocytes, there is a difference between the leucocyte count in the capillary and venous blood in the period following birth, the count in the venous blood being 1000-1500 lower. During the first days of life there is marked neutrophilia and to a lesser extent monocytosis; the period from the 2nd week up to the 4th year is accompanied by lymphocytosis.

Slight neutrophilia occurs towards the end of pregnancy, during physical work, emotional excitement and convulsions, and after taking adrenaline.

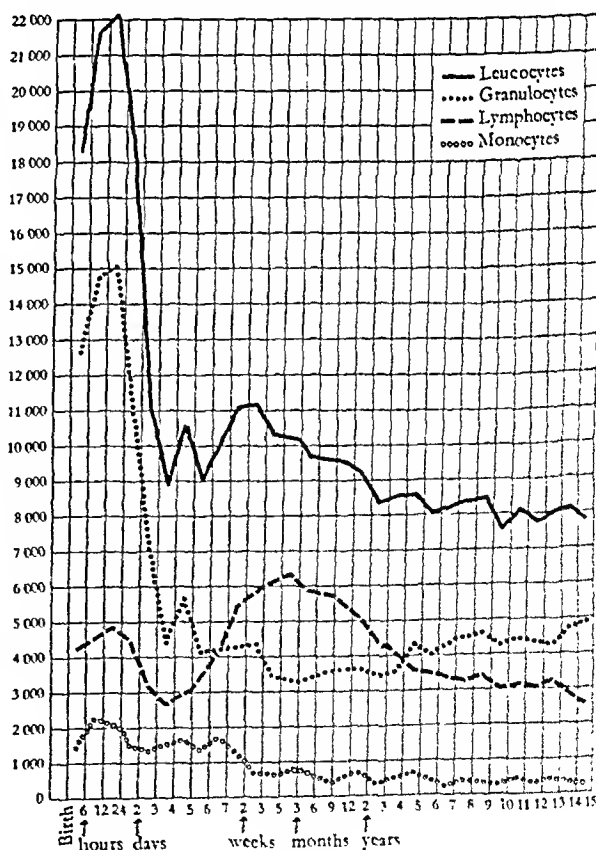
There is no sex difference in the leucocyte count⁸. Daily rhythms as well as seasonal and climatic fluctuations have been reported.

Pathological characteristics

Leucocytosis usually consists of an increase in the number of neutrophils. It occurs in many infectious diseases, in all suppurative conditions due to cocci, in poisoning by various metals and drugs, in diabetic ketosis, in many cases of malignant tumours, in gastric and duodenal ulcers, in gout and in coronary thrombosis. Excessive leucocytosis with a very marked shift to the left in the granulocytes occurs in tuberculous disease with typhoid-like symptoms. Myeloid leukaemia may be variously marked by the presence of myeloblasts, promyelocytes or monocytes, or by a mixture of these cells. Leucocytosis consisting of an increase in the lymphocytes in children is seen mainly in whooping cough and acute infectious lymphocytosis. Leucocytosis due to the presence of lymphoid monocytes is characteristic of infectious mononucleosis.

Leucopenia due to agranulocytosis or granulocytopenia occurs in salmonellosis, in typhoid (more so than in paratyphoid), very occasionally in septicæmia and miliary tuberculosis, in anaphylactic shock and in severe bone-marrow disturbances due for instance

Leucocyte count per microlitre from birth until 15 years⁹



to radiation. Leucopenia consisting of lymphocytopenia or even alymphocytosis is characteristic of many antibody-deficiency syndromes⁹.

(For other physical and chemical data see under 'Blood', pages 557-611)

Total leucocyte counts and distribution at various ages

Age	Ref. case	Total leucocytes	Neutrophil granulocytes		Eosinophil granulocytes	Basophil granulocytes	Lymphocytes		Monocytes		Neutrophil myelocytes*	
			Mean	95% range (extreme range in brackets)	Mean	95% range (extreme range in brackets)	Mean	95% range (extreme range in brackets)	Mean	95% range (extreme range in brackets)	Mean	95% range (extreme range in brackets)
Birth	1	18100	9400	(70-8500)	100	(0-640)	5500	(2000-11000)	1050	(400-3100)	-	0-1908
12 hours	1	22800	13200	(6000-21000)	100	(0-500)	5500	(2000-11000)	58	(400-3600)	-	0-10
24 hours	1	18100	9400	(5000-21000)	100	(0-500)	5500	(2000-11000)	53	(400-3600)	-	-
1 week	1	12260	6300	(3500-10000)	100	(0-250)	5000	(2000-11000)	1100	(200-3100)	-	-
2 weeks	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	58	(300-2700)	-	0-437
4 weeks	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	1100	(200-3100)	-	0-3
2 months	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	1000	(300-2400)	-	0-102
4 months	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	88	(700-2000)	-	-
6 months	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	700	(130-1800)	-	-
8 months	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	650	(100-1500)	-	-
10 months	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	600	(100-1500)	-	-
12 months	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	52	(100-1500)	-	-
2 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	48	(80-1200)	-	-
4 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	47	(50-1200)	-	-
6 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	450	(50-1100)	-	-
8 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	50	(50-1000)	-	-
10 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	450	(0-800)	-	-
12 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	400	(0-800)	-	-
14 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	47	(0-800)	-	-
16 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	380	(0-800)	-	-
18 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	31	(0-800)	-	-
20 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	52	(0-800)	-	-
21 years	1	11400	5800	(3000-10000)	100	(0-250)	5000	(2000-11000)	300	(0-800)	-	-
Adults	1	7000	2800-11200	712-7588	0-397	0-112	2185	1079-3341	456	66-846	0	0

* These cells are also included in the stab neutrophils

* DREXLER, D. S. (Ed.), *Blood and Other Body Fluids*, Federation of American Societies for Experimental Biology, Washington, 1961, page 125

2 FORTMAN, C.E., *Bull. Johns Hopkins Hosp.*, 45, 75 (1929)
3 GRAMER, et al., *Ibid.*, 50, 467 (1955)

(For other physical and chemical data see under 'Blood', pages 557-611)

Basophil count¹⁰*Physiological and pathological characteristics*

1. Increased greatly in chronic myeloid leukaemia and polycythaemia, significantly in diabetes and myxoedema.
2. Decreased greatly in hyperthyroidism, after administration of glucocorticoids and during pregnancy.

Eosinophil count¹¹*Physiological characteristics*

1. Subject to fluctuations at intervals of a few minutes with a range exceeding the error inherent in the method of measurement.
2. Subject to marked daily periodicity with low values in the late afternoon and early morning (down to about 20% of the mean 24-hour value) and a maximum at midnight (up to about 30% of the same mean value). This periodicity is mainly seen in *fasting* subjects.

Schilling's haemogram

Normal relationship of immature neutrophils (myelocytes + young neutrophils + stab neutrophils) to mature (segmented) neutrophils = $\frac{1}{13}$ or less	Basophils	Eosinophils	Myelocytes	Young cells	Stab cells	Segmented cells	Lymphocytes
Normal range (%)	0.5-1.5	2-4	0	0-1	3-5	51-67	20-30

In order to simplify the recording of results of differential counts SCHILLING's haemogram can be written: '-,- / -,-,-,- / -,-', where the dashes represent the percentage values in the order given in the above table of the haemogram. This enables the differential blood picture to be rapidly evaluated.

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Thrombocytes (Platelets)

(For other physical and chemical data see under 'Blood', pages 557-579)

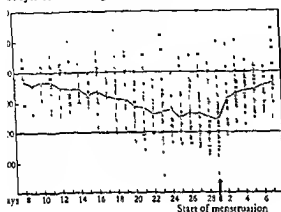
	Mean	95% range (extreme range in brackets)		Reference	Remarks
Thrombocyte count (in thousands per μ l)					
Cord blood	227	149-305	39	1	Determined by the direct method. There are no marked differences as sex or age are concerned ³ . The thrombocyte count is rather low prior to the start of menstruation and rises after cessation of menstruation ⁴ . Differences in the count due to constitution, physical exercise, altitude and ambient temperature have been reported. The thrombocyte count is <i>increased</i> in injury and in chronic myeloid leukaemia, <i>decreased</i> in thrombopenic purpura.
Children					
1 week (cutaneous blood)	233	143-323	45	1	
1 month (cutaneous blood)	277	175-379	51	1	
3 months (cutaneous blood)	348	220-476	64	1	
12 months (cutaneous blood)	339	219-459	60	1	
Adults					
cutaneous blood	250	133-367	58.5	2	
venous blood	310	286-334	11.9	2	
arterial blood	350	322-378	13.9	2	
Thrombocyto-crit value (thrombocyte packing volume) (ml/l)	4.8	(3.3-8.3)	-	5	Proportion of the peripheral venous blood volume occupied by the thrombocytes.
Diameter (μm)	-	(2-4)	-	2, 6	Normally the thrombocytes are spherical or egg-shaped. They undergo change of shape even after brief contact with a wettable surface ^{5, 7} .
Volume (f $\equiv \mu$m³)	-	(10-12)	-	2	Dependent on temperature and on concentration of anticoagulants ⁸ . <i>Increased</i> in thrombopenic purpura and a few other diseases ⁵ .
	16.2	(10.3-19.7)	-	5	
	5.8	-	-	8	Measured by the ³² P-di-isopropyl fluorophosphate (DFP) method. Reduced in polycythaemia vera accompanied by thrombopenia ¹⁰ .
Lifetime (days)	-	(8-14)	-	9	
Half-life (days)	-	(5-6)	-	11	Measured by means of ¹⁴ C-serotonin.
Osmotic resistance	Morphological changes in the thrombocytes occur with NaCl concentration of 0.44% and below; at a concentration of 0.1% almost all the thrombocytes are in the form of ghosts ¹² . The osmotic resistance is lowered in idiopathic thrombocytopenia ¹² , increased in thrombotic conditions ¹² and altered in some infectious diseases ¹³ .

Thrombocytes (Platelets)

(For other physical and chemical data see under "Blood", pages 557-579)

	Mean	95% range	<i>s</i>	Reference	Remarks
Count (per 10 ¹¹ thrombocytes)					
Production per hour	86.3	73.5-99.1	6.4	¹⁴	Values depend on the composition of the incubation medium
Consumption per hour	95.7	74.9-117	10.4	¹⁴	
Formation per hour	3.9	3.1-4.7	0.4	¹⁴	
Formation per hour	76.4	52.6-100	11.9	¹⁴	

Thrombocyte count during menstruation¹⁵



References

- ¹⁴ WALLER et al., *Thrombotic Diathesis haemorrh* (Stuttgart), 3, 520 (1959)
¹⁵ POHLER, F. J., *Amer J med Sci*, 197, 40 (1939)

Bone marrow

Where in haematology we find such conflicting data to be found as the percentages of the various types of cell present in human marrow. This is a result of differences in counting techniques. The greater the amount of marrow aspirated, the greater the volume of blood entering the syringe. The proportions of erythroblasts and

granuloblasts fall while those of the stab and segmented cell lymphocytes rise. The last three types of cell are really constituents of the marrow blood and their numbers can therefore be counted at any time from the peripheral blood. On values in adults see particularly the monograph by ROHM¹.

Diagram at various ages²

Type of cell	24 hours		End of newborn period		Infancy		Early childhood		School age		Adults	
	Range (%)	Mean (%)	Range (%)	Mean (%)	Range (%)	Mean (%)	Range (%)	Mean (%)	Range (%)	Mean (%)	Range (%)	Mean (%)
Erythroblasts												
basophil	0.5-10.0	5.0	0.0-3.0	1.0	0.5-5.0	2.5	1.0-6.0	2.5	1.0-8.0	3.0	0.5-7.5	
polychromatic	7.5-30.0	15.0	0.0-10.0	3.0	5.0-20.0	10.0	3.0-10.0	5.0	3.0-10.0	6.0	2.0-15.0	
oxyphil	7.5-30.0	15.0	2.0-20.0	6.0	5.0-12.5	7.5	5.0-20.0	10.0	5.0-20.0	11.0	5.0-25.0	
Total		35.0		10.0		20.0		17.5		20.0		
Granulopoietic												
Myeloblasts	0.2-5.0	2.5	0.2-5.0	2.0	0.2-5.0	1.5	0.2-5.0	1.0	0.2-5.0	1.0	0.5-5.0	
Promyelocytes	0.2-5.0	3.0	0.5-7.5	3.5	0.5-10.0	2.5	0.5-7.5	2.5	0.5-10.0	3.0	0-7.5	
Myelocytes	2.0-20.0	6.0	5.0-20.0	10.0	5.0-15.0	10.0	5.0-20.0	12.5	5.0-25.0	15.0	5.0-25.0	
Metamyelocytes	5.0-25.0	12.5	5.0-25.0	12.5	5.0-15.0	10.0	5.0-20.0	12.5	5.0-25.0	15.0	5.0-20.0	
Stab cells	5.0-25.0	12.5	10.0-25.0	15.0	5.0-15.0	8.0	5.0-15.0	10.0	5.0-20.0	12.5	5.0-25.0	
Segmented cells	10.0-30.0	15.0	10.0-25.0	15.0	10-15.0	7.0	1.0-15.0	8.5	1.0-15.0	8.0	0.5-15.0	
Eosinophils	0.0-5.0	1.0	0.5-7.5	2.5	1.0-7.5	4.0	1.5-7.5	5.0	1.0-7.0	4.0	1.5-7.5	
Basophils	0.0-0.5	0.05	0.0-1.0	0.05	0-1.0	<0.05	0-0.5	<0.1	0-1.0	<0.2	0-1.0	
Total		52.5		60.0		43.0		52.0		58.5		
Monocytes*	3.0-15.0	7.5	2.0-10.0	5.0	0.5-5.0	2.0	1.0-5.0	3.0	0.5-4.0	1.5	0.5-3.0	
Lymphocytes**												
Reticular cells**	0.0-10.0	5.0	10.0-40.0	25.0	15.0-50.0	35.0	15.0-40.0	27.5	10.0-35.0	20.0	1.5-20.0	
Plasmacytes	0.0-1.0	0.1	0.0-1.5	0.1	0-2.0	<0.5	0-2.5	<0.5	0.2-2.5	0.5	0.5-3.0	
Megakaryocytes		0.1		0.1		<0.5		<0.5		<0.5		

* The high value for monocytes in the marrow of the newborn is probably synchronous with the peripheral monocytosis of the first weeks of life

** Here no distinction is made between lymphoid reticulum and lymphocytes since the data in the literature show large discrepancies

Physiology

The processes involved in the coagulation of blood are still to some extent obscure, so that the diagrammatic representation shown here (Fig. 1) should not be regarded as conclusive.

Normally, the blood begins to coagulate when it escapes as a result of injury to a vessel and comes into contact with a foreign, wettable surface, for instance damaged tissue. In the presence of calcium ions, contact of the blood with such a surface results in the activation of Factor XII, which in turn initiates the viscous metamorphosis of the thrombocytes in a manner as yet unknown. The thrombocytes become labile, and as a consequence agglutinate to the foreign surface, to one another and to other cells. The result is the formation of a platelet thrombus and the release of a number

causes the activation in succession of Factors XI, IX, VIII and X in a chain reaction. The activated Factor X, together with the lipoid factor of the thrombocytes, forms active plasma thromboplastin (the so-called intrinsic system).

Factor X is likewise activated in the presence of calcium ions by the tissue fluid in conjunction with Factor VII. The Factor X activated by this system (the so-called extrinsic system) brings about the formation of active tissue thromboplastin. The formation of both these active thromboplastins is accelerated by Factor V.

In the first phase of coagulation the two active thromboplastins – plasma thromboplastin and tissue thromboplastin – act on the prothrombin and convert it into thrombin.

Heparin inhibits the activity of both the thromboplastins and thrombin. At this stage other antithrombins likewise function as antagonists in the coagulation process.

In the second stage of coagulation thrombin acts on the fibrinogen, which is thereby converted into monomeric, soluble fibrin. The latter now polymerizes and is converted under the action of Factor XIII and calcium ions into stable fibrin.

In the third phase the fibrin clot undergoes retraction under the action of the agglutinated thrombocytes.

The retracted clot may eventually be broken down by plasmin to yield soluble products. Plasmin is a rather nonspecific proteolytic enzyme; under pathological conditions it is also capable of breaking down fibrinogen and other protein components of the coagulation system. Plasmin is formed from plasminogen as a result of a complicated series of activation processes, commencing with the formation of an activator by the action of lysokinases – present in both blood and tissues – on a proactivator of the blood. This activator converts plasminogen into plasmin. The latter can also arise from plasminogen directly via a tissue activator. Lysokinases are inhibited by antilyso kinases, plasmin activity by anti-plasmin.

Physiological variations

The coagulation process does not function fully in all newborn children. On the average, the concentrations of fibrinogen and Factors II, VII, IX and X are low, especially during the first few days of life; there are considerable individual variations, however, and values above normal may even be encountered¹.

The number and functional state of the thrombocytes are both within the normal range in newborn infants, both full-term and premature (see also page 620).

Ageing as such does not appear to involve any alteration in the coagulation process. Pathological changes are probably in most cases due to changes in either the coagulation process or the vessels. Impairment of the coagulation system due to certain foodstuffs appears to be commoner in old age; an example is the increased tendency to coagulation after a meal rich in fats².

During pregnancy the concentrations of Factors VII and X in the blood are often increased. The occasional rise in the blood levels of Factor IX and fibrinogen, combined with an enhanced tendency of the thrombocytes to agglutinate in the presence of an increased blood phospholipid concentration, may lead to thrombo-embolic complications during pregnancy³.

Pathology

The pathology of blood coagulation comprises three main types of disease: thrombosis with the concomitant danger of embolism, the haemorrhagic diatheses, and cardiac infarction.

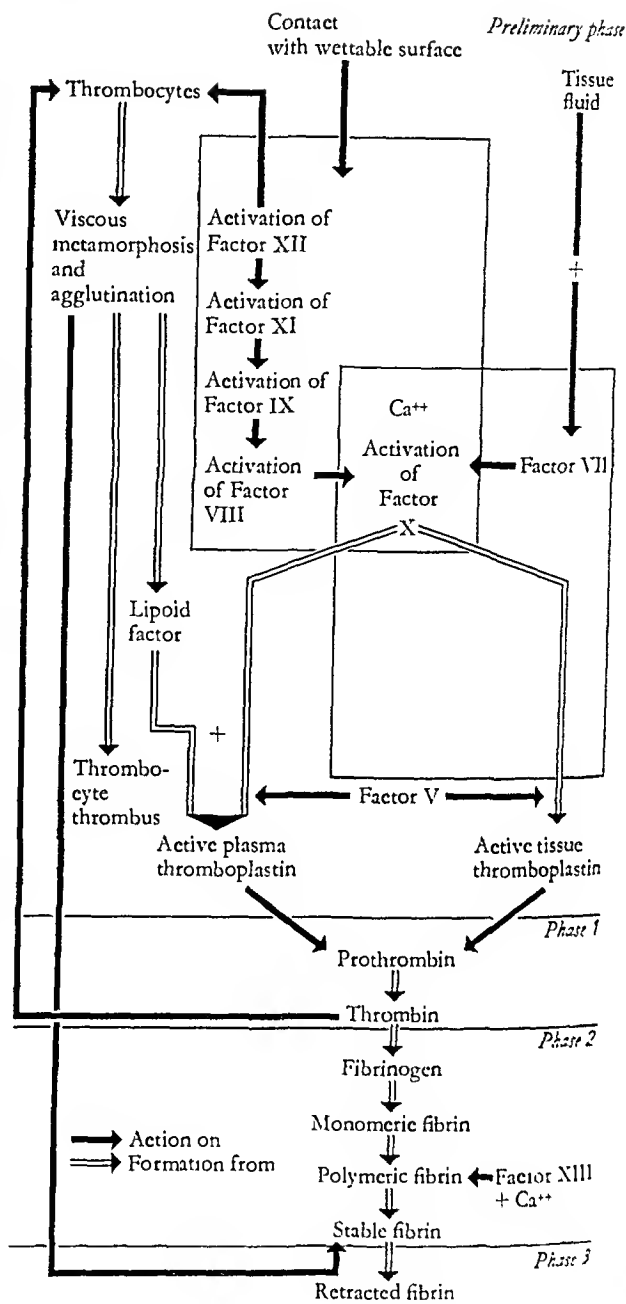


Fig. 1

Thrombo-embolism

In the vessels, plasmatic coagulation of the blood can come about through exhaustion of the endogenous heparin or, in general, through a reduction in the antithrombin level.

Lowering of platelet stability through activation of Factors XII and X (for instance as a result of pathological changes in the vascular wall) or following some specific thrombocytic disease can likewise enhance the tendency to coagulation. The same result can come about through inhibition of the fibrinolytic system by physiological inhibitors, drugs or disease. Stasis due to a diminished rate of blood flow also favours thrombosis.

The sites where thromboses are most likely to occur are shown in order of frequency in Figure 2.

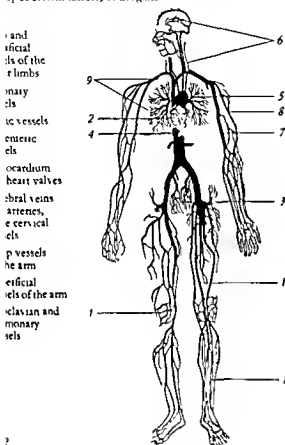
Theoretically feasible methods of treatment are first a reduction in the plasmatic coagulation potential by means of oral anticoagulants, secondly inhibition of the activity of the thromboplastins and thrombin by means of heparin, thirdly stabilization of the thrombocytes, i.e., inhibition of the contact activation process (inhibition of the activity of Factor XII), and lastly an increase in fibrinolytic activity.

* This chapter (pages 622-625) has been compiled by C. MONTIGEL, Research Laboratories of J. R. Geigy S.A., Basle (Switzerland).

hagic diatheses

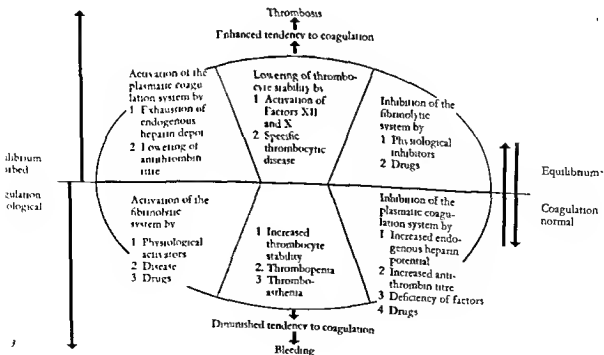
Increased tendency to bleeding may be due to an abnormality in fibrinolytic activity (caused by physiological activators, or drugs), to enhanced stability of the thrombocytes, to cytopenia or hereditary thrombo-saethenia, and finally to an abnormality of the plasmatic coagulation process as a result of an endogenous heparin, a rise in the antithrombin titre, a deficiency of certain factors, or drug action

Plasmatic coagulation system by an excess of endogenous heparin or heparin-like inhibitors can be overcome by administering prota-

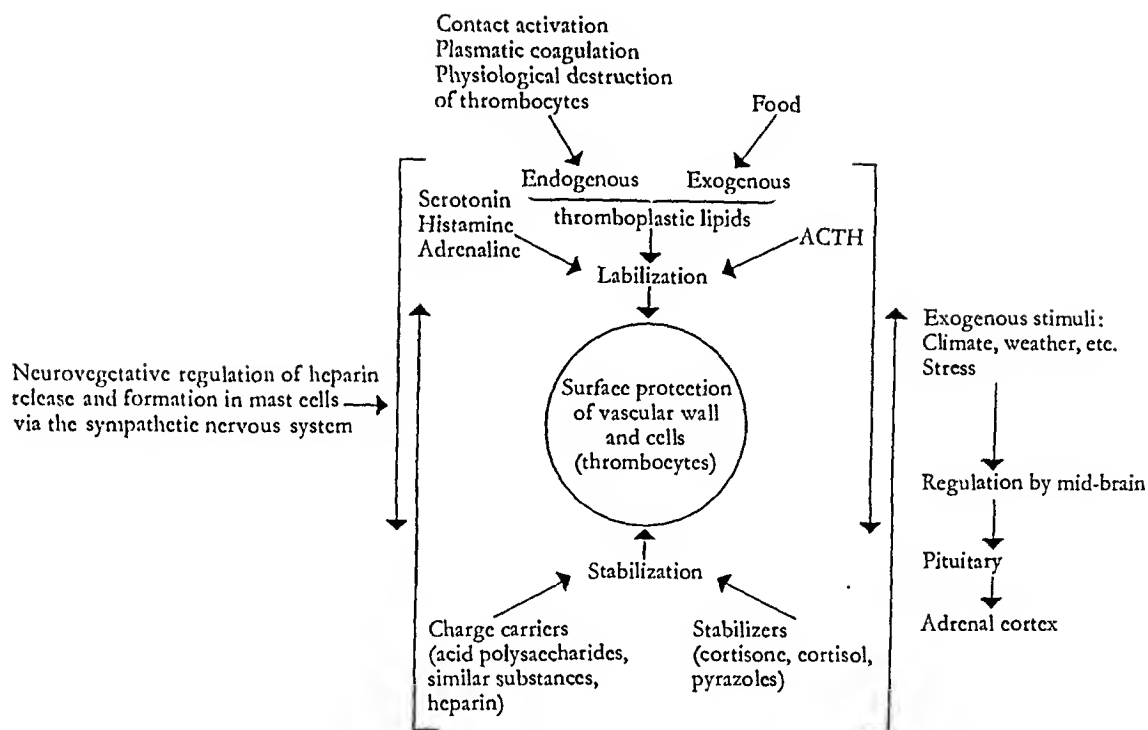


Cardiac infarction

In spite of certain common external causes and initiating mechanisms, the pathogenesis of cardiac infarction differs considerably from that of thrombosis. Only in rare cases are primary coagulation thrombi found in cardiac infarction. Many aspects of the disease are still unexplained.



Blood Coagulation



results in the formation of necrotic areas in the vascular walls and in the heart, particularly beneath the endocardium, in the wall of the left ventricle, in the septum and in the apex, in fact in any part where a high concentration of monoamine oxidase can be demonstrated histologically⁵. This necrosis causes a manifest infarct either directly or via the development of oedema in the coronary vessels. The action of catecholamines in causing necrosis, oedema and thus infarction is also favoured by the hypertension, spasms, stasis and ischaemia that commonly result from a disturbance of haemodynamics and cardiac activity.

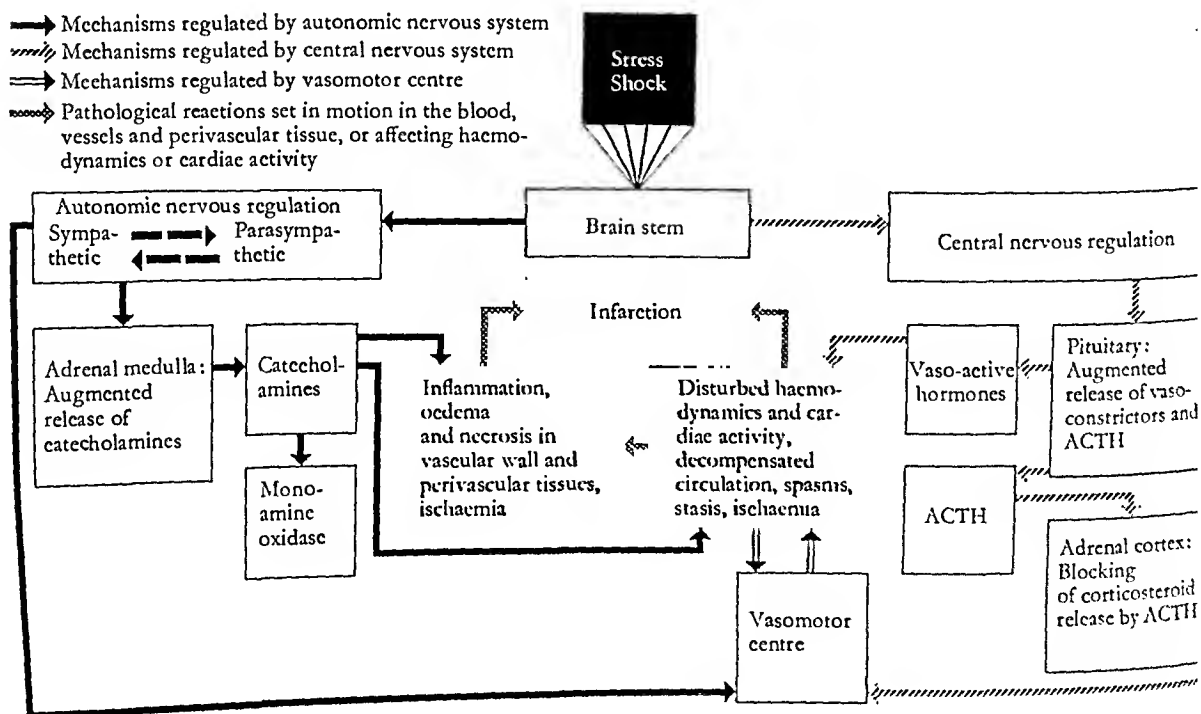
The process of infarction initiated in this way is intensified by mechanisms under central nervous control and mediated by the pituitary and vasomotor centre⁶. The pituitary releases larger amounts of vasoconstrictor substances, with the result that the

haemodynamic equilibrium is disturbed. At the same time regulation of cardiac activity and of haemodynamics by the motor centre is impaired. The increased release of ACTH by the pituitary blocks the release of corticosteroids by the adrenal, so that the stability of the vascular wall is endangered (Fig.

Methods

The coagulation process can be studied by various routine methods suitable for any laboratory:

Bleeding time. Measured by making a small wound in a capillary small vein or arteriole. The results depend on the condition of the plasma, thrombocytic and fibrinolytic coagulation systems. Interruption is not possible.



Recalcification time. This method is particularly useful for measuring the effect of heparin and heparinoids on the plasmatic coagulation system.

it since it is modified in certain thrombocytic diseases as well as using treatment with heparin

Heparin tolerance test. By measuring the coagulability of the blood this test makes it possible to assess the patient's tendency to thrombosis

A number of *special methods*, suitable only for appropriately equipped laboratories, are available for determining individual factors and functions involved in the physiological coagulation process. They require the use of either expensive apparatus like the thrombo-elastograph and thrombocyte aggregometer or special

reagents which must be prepared in the laboratory itself. The special methods whose reliability is now established are listed in the table below. For a detailed description of the techniques involved see MONTGEL².

References

- ¹ McELFRESH, A. E., *Amer J med Sci*, 242, 771 (1961), SILKO, N. A., quoted in *Abstr. Fed Med*, 33, 74 (1963), LANDRECH, G., in WIESENER, H. (Ed) *Einführung in die Entwicklungsphysiologie des Kindes*, Springer, Berlin, 1961, page 118

Special methods of studying blood coagulation

Phase of coagulation	Factor or phase tested	Method	Reagent	Remarks
Preliminary phase, intrinsic system, thrombocytic process	Thrombocyte function	Thrombo-elastograph Thrombocyte aggregometer (BAEDDIN's method)		
Preliminary phase, intrinsic system, plasmatic process	Contact activation Factor XII	Thrombo-elastograph Thrombocyte aggregometer		
Preliminary phase, intrinsic system, plasmatic process	Factor X	Measurement of coagulation	Factor X-free plasma + viper toxin + phospholipids	Only when Factor VII is present in adequate amount
extrinsic system, plasmatic process			Factor X-free plasma + tissue thromboplastin	
Preliminary phase, extrinsic system	Factor VII	Measurement of coagulation	Factor VII-free plasma + tissue thromboplastin	
Preliminary phase, plasmatic process	Factor V	Measurement of coagulation	Factor V-free plasma + tissue thromboplastin	
Preliminary phase, plasmatic process, inhibitors	Antithrombin II	Measurement of coagulation after addition of fibrinogen	Fibrinogen solution	
Phase 1	Factor II Prothrombin	Measurement of coagulation	Factor II-free plasma + tissue thromboplastin	
Phase 2	Factor I			No satisfactory routine method
Phase 3	Retraction potential of thrombocytes	Measurement of clot retraction		
Phase 4	Fibrinolytic potential	Plasmolysis time		

Blood Groups*

(For references see pages 633-634)

The blood groups¹ consist of inherited characters of the blood corpuscles, particularly the erythrocytes, identifiable as antigens by means of their reaction with specific antibodies. The genes responsible for the presence of these antigens are inherited in accordance with Mendelian principles. Most of the blood-group characters are already identifiable in the young embryo and remain unchanged throughout life. They are unaffected by external factors like climate or, in general, disease².

The blood-group characters can be arranged into systems, those so far recognized being the AB0, MNSs, P, Rh, Lutheran, Kell, Lewis, Duffy, Kidd, Diego, Ii, Auerger, Xg, Yt and Dombrock systems. With one exception, each of these systems is inherited independently of the others as an autosomal character; the exception is the Xg group, which is located on the X chromosome. Also known are blood-group antigens of very rare occurrence ('private antigens'), like the Levay, Jobbins, Becker, Ven, Rm, Chr^a, Wra, Be^a, By, Sw^a, Good, Bi and Tra antigens, as well as others only rarely absent from human erythrocytes, like Vel, Ge, Lan and Sm ('public antigens').

An individual's blood-group characters are identifiable by means of antibodies. These may be of human origin either agglutinins or incomplete antibodies. The antibodies are either naturally occurring, i.e., they have not arisen from any known immunizing stimulus, or they are immune antibodies due to an immunizing stimulus such as pregnancy or blood transfusion or injection. Test sera containing hetero-antibodies may also be produced by immunizing suitable animals. Finally, certain reagents of vegetable origin (phytagglutinins) can be used to identify particular blood-group characters (A₁, A₂, H, M, N, etc.).

An antigen-antibody reaction takes place between the test serum and the antigen-carrying erythrocytes leading either to agglutination or, occasionally, in the presence of complement, to haemolysis.

At the right temperature, the agglutinins react with erythrocytes suspended in physiological salt solution. Reaction with incomplete antibodies may be demonstrated

(a) in viscous reaction media, 22-30% beef albumin being a particularly suitable one; other substances used for this purpose include human serum or plasma free of antibodies, gelatin, dextran, polyvinylpyrrolidone, gum arabic, etc.

(b) in the fermentation test; in the main the following proteolytic enzymes are used: trypsin, papain, bromelain and ficin.

(c) in the indirect antiglobulin test (COOMBS' test).

Combinations of tests (for instance a trypsin test combined with an indirect antiglobulin test) are particularly sensitive.

The AB0 blood-group system (LANDSTEINER, 1900³)

The iso-antibodies anti-A and anti-B are normal and regular constituents of appropriate human blood sera. Two antigens (agglutinogens) A and B, reacting respectively with anti-A and anti-B, enable an individual's blood to be assigned to one of the four groups A, B, AB or 0.

Table 1

Reaction with anti-A . . .	+	-	+	-
Reaction with anti-B . . .	-	+	+	-
Blood group	A	B	AB	0

The antigen is located on the surface of the erythrocytes, while the serum contains the iso-antibody, either anti-A or anti-B, corresponding to the antigen not carried by the erythrocytes; if both antigens are carried, or both lacking, the serum contains respectively neither iso-antibody, or both:

Table 2

Blood group	Antigen carried by erythrocytes	Antibodies in serum
0	-	anti-A + anti-B
A	A	anti-B
B	B	anti-A
AB	A and B	neither

From the genetic aspect, an allelic gene (A, B or 0) is a chromosomal locus, the blood group being determined by the combined effect of the two genes situated at the equi-phenotypically, the character 0 is found only in the homozygous form.

The four blood groups (phenotypes) arise from the six genotypes, as shown in Table 3. It is impossible to distinguish logically between AA and AO or between BB and BO.

Table 3

Blood group (phenotype)	Genotype
0	00
A	AA or AO
B	BB or BO
AB	AB

The frequencies with which the various blood groups within a population differ widely. From these phenotypes the corresponding gene frequencies can be calculated (see RACE and SANGER⁴). Such data are of great interest in anthropological studies.

Subgroups of the ABO system

The blood group A can be subdivided into A₁ and A₂B. Anti-A sera (from B individuals) consist of two components: anti-A₁ and anti-A₂. Anti-A₁ reacts only with erythrocytes of A₁ and A₁B, anti-A₂ on the other hand with groups A₁, A₂, A₂B. This subdivision of A increases the number of possible blood groups from four to six, namely 0, A₁, A₂, B, A₁B, A₂B. There are 10 genotypes corresponding to these phenotypes (

Table 4

Blood group (phenotype)	Genotype
0	00
A ₁	A ₁ A ₁ , A ₁ A ₂ , A ₁ 0
A ₂	A ₂ A ₂ , A ₂ 0
B	BB, B0
A ₁ B	A ₁ B
A ₂ B	A ₂ B

Anti-A₁ is present as an irregular antibody in the serum of A₂ individuals and about 26% of A₂B individuals.

Table 5 summarizes the serological data of the A₁A₂B0

Table 5

Blood group	Reaction with test serum			Antibodies regularly present in serum	Antibodies occasionally present in
	anti-A	anti-A ₁	anti-B		
0	-	-	-	anti-A (+ anti-A ₁) anti-B	-
A ₁	+	+	-	anti-B	-
A ₂	+	-	-	anti-B	anti-A ₁ in about 1
B	-	-	+	anti-A (+ anti-A ₁)	-
A ₁ B	+	+	+	none	-
A ₂ B	+	-	+	none	anti-A ₁ in about 2

The A subgroups can also be determined by means of phytagglutinins. *Delichos biflorus* extract reacts specifically with A₁, an extract of *Lotus tetragonolobus* seeds can be used as anti-A₂ reagent.

* The chapters on 'Blood Groups' and 'Serum Groups' (pages 626-634) have been compiled by L. P. HOLLÄNDER, Blood Donor Centre of the Swiss Red Cross, Basle.

ry rare cases a blood cannot be assigned to one of the A subgroups, when it is assumed to belong to an intermediary subgroup (A₂).

Table 6

Test serum	A ₁	A ₂	A ₃	A _x	A _m
action with test sera					
anti-A (blood group B)	+	+	++	-(+)	-(+)
anti-A+B (blood group O) ...	+	+	++	+	-(+)
anti-A ₁	+	-	-	-	-
action of serum with erythrocytes					
A ₁	-	(+)	-	+	✓
A ₂	-	-	-	-	✓
B	+	+	+	+	+
A' substance present in saliva of secretors	Yes	Yes	Yes	No	Yes

* Mixed agglutination

In the serum of Rh-negative individuals

and leucocytes. The chemical constitution of the A, B and H group substances has been largely elucidated

The MNs blood-group system (LANDSTEINER and LEVINE, 1927¹⁰)

The M and N antigens of human erythrocytes can be identified by means of heterospecific immune sera from rabbits. Phenotypes and genotypes of the M and N properties are shown in Table 7

Table 7

Reaction with anti-M	+	+	-
Reaction with anti-N	-	+	+
Phenotype (blood group)	M	MN	N
Genotype	MM	MN	NN

enables nine genotypes to be distinguished (Table 8). The genotypes *MS/Ns* and *Mi/NS* cannot be distinguished serologically

Table 8

	<i>MS/MS</i>	<i>MS/Mi</i>	<i>Mi/Mi</i>	<i>MS/NS</i>	<i>Mi/NS</i>	<i>MS/Ns</i> or <i>Mi/NS</i>	<i>NS/NS</i>	<i>NS/Ns</i>	<i>Ns/Ns</i>
anti-M ...	+	+	+	+	+	+	-	-	-
anti-N ...	-	-	-	+	+	+	+	+	+
anti-S ...	+	+	+	-	-	-	+	+	+
anti-s ...	-	-	-	+	+	+	-	-	-

Weak forms of M or N (*M_s*, *N_s*) are occasionally met with. They are characterized by reacting only weakly with anti-M or anti-N sera. *M_s* (DUNSFORD et al.¹²) reacts with most anti-M and some anti-N sera and is considered to be intermediate between M and N. The *M₁* antigen (JACK et al.¹⁴) is qualitatively different from M and is

samples except those that were negative to anti-S and anti-s. This so-called anti-U behaves like an inseparable mixture of anti-S and anti-s. Individuals who form anti-U possess neither S nor s. The

an allele of M or N, S or s, though also forming part of the MNs complex. Further antigens belonging to this system are R₁¹⁶ and S₁¹⁶ (CLEGHORN²⁴), M₁²⁵, C₁²⁶ and N₁²⁷

The P blood-group system (LANDSTEINER and LEVINE, 1927¹⁰)

Human bloods react either positively or negatively with anti-P sera. In the serum of P-negative individuals there is a substance which reacts with anti-P sera

Table 9

	Phenotype	Genotype
anti-P	+	P+ PP or Pp
	-	P- pp

T
w
z
a

Table 10

Reaction with anti-P ₁ (anti-P)	+	—	—
Reaction with anti-P + P ₁ (anti-Tj ^a)	+	+	—
Genotype	P ₁ P ₁ (PP) P ₁ P ₂ (Pp) P ₁ p (PTj ^b)	P ₂ P ₂ (pp) P ₂ p (pTj ^b)	pp (Tj ^b Tj ^b)
Phenotype	P ₁	P ₂	p
The designation in brackets is that usual prior to 1955.			

The Rhesus blood-group system (LANDSTEINER and WIENER, 1940³²)

The discovery of the Rh blood-group system proved to be of great practical importance in view of the fact that Rh-negative persons form Rh antibodies fairly frequently after contact with the Rh antigen (transfusion or injection of blood, pregnancy). A second transfusion with Rh-positive blood may result in a haemolytic transfusion reaction. In women the result may be haemolytic disease in her newborn children (LEVINE et al., 1941¹¹⁹). For clinical purposes the distinction between Rh-positive and Rh-negative is usually sufficient, but in fact the Rh blood-group system is extremely complex. This complexity is one of the reasons why various genetic explanations of the Rh groups have been put forward and at least three different nomenclatures are in use. WIENER's concept³³ assumes the existence of a single gene locus on the chromosome with multiple alleles. Each allele results in the formation of an agglutinin possessing several factors. These factors act as antigens and can be detected by means of the corresponding antibodies. On the other hand, according to FISHER and to RACE³⁴ the Rh group to which a blood belongs is determined by three closely linked gene pairs. Each individual inherits three Rh genes from his parents, namely *C* or *c*, *D* or *d* and *E* or *e*, in the form of an indivisible gene complex. For instance, an individual inherits *CDe* from one parent and *cde* from the other. Table 11 (from RACE and SANGER¹) illustrates the two concepts using *CDe* as an example.

Table 11

	Gene	Agglutinin	Factors	Antibodies
WIENER	<i>R¹</i>	<i>Rh₁</i>	<i>Rh₀</i>	anti- <i>Rh₀</i>
			<i>rh'</i>	anti- <i>rh'</i>
			<i>hr''</i>	anti- <i>hr''</i>
FISHER and RACE	<i>C</i>	<i>C</i>		anti- <i>C</i>
	<i>D</i>	<i>D</i>		anti- <i>D</i>
	<i>e</i>	<i>e</i>		anti- <i>e</i>

The correspondence between WIENER's factors and the antigens of FISHER and RACE, together with that between the respective antibodies, is shown in Table 12.

Table 12

<i>Rh₀</i> = D	anti- <i>Rh₀</i> = anti-D
<i>rh'</i> = C	anti- <i>rh'</i> = anti-C
<i>rh''</i> = E	anti- <i>rh''</i> = anti-E
<i>hr'</i> = c	anti- <i>hr'</i> = anti-c
<i>hr''</i> = e	anti- <i>hr''</i> = anti-e

Antigens have since been discovered which correspond partially to further alleles on the same single gene locus.

Alleles and variants of *D*

STRATTON³⁵ has described the antigen *D^u*, which reacts positively with some anti-*D* sera, negatively with others. *D^u* occurs in various

strengths (high-grade and low-grade) and appears to be identical with WIENER's intermediate form (*Rh₀*). In *D^u* individuals the antigen *D* can cause the formation of anti-*D*. The fact that *D*-positive individuals can also form anti-*D* (ARGALL et al.³⁶) led WIENER and UNGER³⁷ to assume the existence of partial antigens of *D*. Individuals not possessing one of these partial factors can form antibodies against it. *Rh^a* indicates a blood in which the partial factor *Rh^A* is missing and which reacts with anti-*Rh₀* and also with anti-*Rh^B*, anti-*Rh^C* and anti-*Rh^D*. These variants and their reactions are shown in Table 13.

Table 13

Variant	Reaction with				
	anti- <i>Rh₀</i>	anti- <i>Rh^A</i>	anti- <i>Rh^B</i>	anti- <i>Rh^C</i>	anti- <i>Rh^D</i>
<i>Rh^a</i>	+	—	+	+	+
<i>Rh^b</i>	+	+	—	+	+
<i>Rh^c</i>	+	+	+	—	+
<i>Rh^d</i>	+	+	+	+	—
<i>Rh^{ab}</i>	+	—	—	+	+
<i>Rh^{abc}</i>	+	—	—	—	+
<i>Rh^{ac}</i>	+	—	+	—	+

The antigen described by CHOWN et al.³⁸ as reacting with the antibody anti-*Wiener* appears to be a further partial antigen of *D^u*.

Alleles and variants of *C* and *c*

C^w (CALLENDER and RACE³⁹) is a third allele and reacts with a specific anti-*C^w* serum. Most anti-*C* sera also possess an anti-*C^w* component. A rare and weakly reacting antigen is *C^u* (RACE et al.⁴⁰), a parallel to *D^u*. Anti-*C^u* is a not very rare antibody reacting with the very rare antigen *C^x* (STRATTON and RENTON⁴¹).

Alleles and variants of *E* and *e*

The antigen *E^u* (CEPELLINI et al.⁴²) is analogous to *D^u* and *C^u*. *E^w* (GREENWALT and SANGER⁴³) has so far been found only in a very few families, *e^s* (SANGER et al.⁴⁴) only in members of the negro race. SHAPIRO⁴⁵ found the antibody anti-*hr^s* in the serum of a Bantu woman; the factor *hr^s* occurs not only among the Bantu but also in white races. The antigen *eⁱ* was found among the Columbian Indians (LAYRISSE et al.⁴⁶).

Table 14 shows WIENER's analysis of the Rh phenotypes occurring in the white population of New York City⁴⁷, Table 15 their distribution among the English people as determined by RACE et al.⁴⁸.

During the last few years compound antigens of the Rh system have been discovered, for instance *ce*, which reacts with the anti-serum originally designated anti-*f* (ROSENFELD et al.⁴⁹). Other compound antigens are *rh₁* or *Cc* (ROSENFELD and HABER⁵⁰), *CE* (TIPPETT et al.⁵¹) and *ce^s*, which reacts with the serum originally designated anti-*V* (DENATALE et al.⁵²). The antigen *G* described by ALLEN and TIPPETT⁵³ is not a compound antigen in the same sense; it is closely related to *C* and *D*, since most *C*- or *D*-positive individuals are also *G*-positive. Anti-*G* is found in the serum of *cde* and *cdE* individuals, most of whom also form the antibody anti-*D* + *C*.

The first case of a 'deficient' Rh chromosome was described by RACE et al.⁵⁴ and designated by them —*D*— (*Rh₀* in WIENER's nomenclature). Others have since come to light, namely *C^wD*— (GUNSON and DONOHUE⁵⁵), *cD*— (TATE et al.⁵⁶), —— (*Vos* et al.⁵⁷). It is not known whether these are cases of gene suppression or gene depression.

The antigen contents of the individual gene complexes are summarized in Table 16 (page 631) (from RACE and SANGER¹).

An Rh complex with gene depression has been given the designation *r⁰* (ALLEN and TIPPETT⁵³). Similar behaviour is shown by the antigens of the complexes *r^M* (TIPPETT et al.⁵¹) and *r^L* (METAXAS and METAXAS-BÜHLER⁵⁸).

In 1962, ROSENFELD et al.⁵⁹ proposed a new terminology for the Rh groups in which the Rh antibodies were given numbers in the chronological order of their identification. The original publication listed 21 antibodies, since when the number has risen to 27 (KEITH et al.⁶⁰). This nomenclature is without prejudice to any

Table 14 Rh—its phenotypes and genotypes

Table 14 Rh-16 polymorphism among Negroes

2 Rh phenotypes			12 Rh phenotypes			24 Rh-16 phenotypes				55 genotypes	
Designation	Type	Approximate frequency among New York City whites %	Reaction with anti Rh ₁ or anti Rh ₂	Reaction with anti-rh ⁺		Designation	Approximate frequency among New York City whites %	Reaction with anti hr ⁺			
				anti-rh ⁺	anti-rh ⁺ anti rh ⁺			anti hr ⁺	anti-hr		
Rh-negative	rh	14.4	—	—	—	rh	14.4	+	+	rr	
	rh'	0.46	+	—	—	rh'rh	0.46	+	+	r'r	
						rh'rh'	0.036	—	—	r'r'	
	rh ⁺	0.004	+	—	+	rh ⁺ rh	0.004	+	+	r ⁺ r ⁺ or r ⁺ r ⁺	
						rh ⁺ rh'	0.00006	—	—	r ⁺ r ⁺ or r ⁺ r ⁺	
	rh ⁺	0.38	—	+	—	rh ⁺ rh	0.38	+	+	r'r	
						rh ⁺ rh'	0.0025	+	+	r'r'	
	rh ₁	0.01	+	+	—	rh ₁ rh	0.006	+	+	r ⁺ r ⁺	
						rh ₁ rh'	0.008	+	+	r ⁺ r ⁺	
						rh ₁ rh ₁	0.0001	—	—	r ⁺ r ⁺	
Rh-positive	rh ₁ ⁺	0.0005	+	+	+	rh ₁ ⁺ rh	0.00005	+	+	r ⁺ r ⁺	
						rh ₁ ⁺ rh'	0.00001	—	—	r ⁺ r ⁺	
	Rh ₁	2.1	—	—	—	Rh ₁	2.1	+	+	R ₁ R ₁ or R ₁ r	
						Rh ₁ rh	33.4	+	+	R ₁ r, R ₁ R ₁ or R ₁ r	
						Rh ₁ Rh ₁	17.3	—	—	R ₁ R ₁ or R ₁ r	
	Rh ₁ ⁺	3.3	+	—	+	Rh ₁ ⁺ rh	1.6	+	+	R ₁ r, R ₁ R ₁ or R ₁ r	
						Rh ₁ ⁺ rh ₁	1.7	—	—	R ₁ R ₁ , R ₁ r ⁺ , R ₁ r ⁺ , R ₁ r ⁺ or R ₁ r ⁺	
	Rh ₂	14.6	—	+	—	Rh ₂ rh	12.2	+	+	R ₁ r, R ₁ R ₁ or R ₁ r	
						Rh ₂ Rh ₂	2.4	+	+	R ₁ R ₁ or R ₁ r	
	Rh ₂ ⁺	13.4	+	+	—	Rh ₂ rh ₁	12.9	+	+	R ₁ R ₁ , R ₁ r ⁺ or R ₁ r ⁺	
						Rh ₂ rh	0.2	+	+	R ₁ r, R ₁ R ₁ or R ₁ r	
						Rh ₂ Rh ₁	0.2	—	—	R ₁ R ₁ , R ₁ r ⁺ or R ₁ r ⁺	
						Rh ₂ rh ₂	0.07	+	+	R ₁ R ₁ , R ₁ r ⁺ or R ₁ r ⁺	
						Rh ₂ Rh ₂	0.0004	—	—	R ₁ R ₁ or R ₁ r	
	Rh ₂ ⁺	0.6	+	+	+	Rh ₂ ⁺ rh ₁	0.6	+	+	R ₁ R ₁ , R ₁ r ⁺ or R ₁ r ⁺	
						Rh ₂ ⁺ rh ₂	0.008	—	—	R ₁ R ₁ , R ₁ r ⁺ or R ₁ r ⁺	

Table 15 The Rh genotypes of English people (from RACE et al.⁴⁰)

Calculated group frequency (if only first 4 sera used) %	Reaction with the 4 antisera fairly widely available				Reaction with rarer antisera					Genetic and antigenic constitution	Short symbols		Calculated genotype frequency %
	CC ^w	c	D	E	pure C	pure C ^w	c	f	d		much used	WIENER and WEXLER ⁴⁷	
15.1020	—	+	—	—	—	—	+	+	+	cde/cde	rr	rr	15.1020
2.0609	—	+	+	—	—	—	+	+	—	cDe/cde cDe/cDe	R ⁰ r R ⁰ R ⁰	R ⁰ r R ⁰ R ⁰	1.9950 0.0659
0.9376	—	+	—	+	—	—	+	+	+	cdE/cde cdE/cdE	R ⁰ r R ⁰ R ⁰	r ⁰ r r ⁰ r ⁰	0.9235 0.0141
14.0769	—	+	+	+	—	—	—	—	—	cDE/cDE cDE/cdE cDE/cDe cDE/cde cDe/cde	R ₂ R ₂ R ₂ R ⁰ R ₂ R ⁰ R ₂ r R ⁰ R ⁰	R ⁰ R ⁰ R ⁰ r ⁰ R ⁰ R ⁰ R ⁰ r ⁰ R ⁰ r ⁰	1.9906 0.3353 0.7243 10.9657 0.0610
0.7644	+	+	—	—	+	—	+	+	+	Cde/cde C ^w de/cde	R ⁰ r R ⁰ r ⁰	r ⁰ r r ⁰ r ⁰	0.7644 0.0000
34.8899	+	+	+	—	+	—	+	+	—	CDe/cDe CDe/cde cDe/Cde C ^w De/cDe C ^w De/cde C ^w de/cDe	R ₁ R ₀ R ₁ r R ₀ R ⁰ R ⁰ R ₀ R ⁰ r R ⁰ r ⁰	R ⁰ R ⁰ R ⁰ r R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ R ⁰ r ⁰ r ⁰ r ⁰	2.0922 31.6759 0.0505 0.0664 1.0049 0.0000
0.0234	+	+	—	+	+	—	+	+	+	cdE/Cde CdE/cde CdE/cDe C ^w de/cDe	R ⁰ R ⁰ R ₀ r R ₀ R ⁰ R ⁰ r ⁰	r ⁰ r ⁰ r ⁰ r r ⁰ r ⁰ r ⁰ r ⁰	0.0234 0.0000 0.0000 0.0000
13.4178	+	+	+	+	+	—	+	—	—	CDe/cDE cDe/CDE CDe/cdE cDe/Cde CDE/cde CdE/cDe cDE/CDE cdE/CDE CdE/cDE C ^w De/cDE C ^w De/cde C ^w de/cDE C ^w de/CDE	R ₁ R ₂ R ₀ R ₂ R ₁ R ⁰ R ₂ R ⁰ R ₂ r R ₀ R ₀ R ₂ R ₂ R ⁰ R ₂ R ₀ R ₂ R ⁰ R ₂ R ⁰ R ₂ R ⁰ r ⁰ R ⁰ r ⁰	R ⁰ R ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰	11.5000 0.0125 0.9685 0.2775 0.1893 0.0000 0.0687 0.0058 0.0000 0.3648 0.0307 0.0000
0.0097	+	—	—	—	+	—	+	—	+	Cde/Cde C ^w de/Cde C ^w de/C ^w de	R ⁰ R ⁰ R ⁰ r ⁰ R ⁰ r ⁰	r ⁰ r ⁰ r ⁰ r ⁰ r ⁰ r ⁰	0.0097 0.0000 0.0000
18.5073	+	—	+	—	+	—	+	—	—	CDe/CDe CDe/Cde CDe/C ^w De C ^w De/Cde C ^w de/CDe C ^w De/C ^w De C ^w de/C ^w De	R ₁ R ₁ R ₁ R ⁰ R ₁ R ⁰ R ⁰ R ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰	R ⁰ R ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰	16.6097 0.8016 1.0539 0.0254 0.0000 0.0167 0.0000
0.2101	+	—	+	+	+	—	+	—	—	CDe/CDE Cde/CDE CdE/Cde CDE/CDE C ^w De/CDE CdE/CDE CdE/C ^w De C ^w de/CDE	R ₁ R ₂ R ⁰ R ₂ R ₀ R ₁ R ₂ R ₂ R ₁ R ₂ R ₀ R ₂ R ₀ R ₁ R ⁰ R ₂	R ⁰ R ⁰ r ⁰ r ⁰ r ⁰ r ⁰ R ⁰ R ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰ R ⁰ r ⁰	0.1985 0.0048 0.0000 0.0006 0.0062 0.0000 0.0000 0.0000
0.0000	+	—	—	+	+	—	+	—	+	CdE/Cde CdE/Cde CdE/C ^w de	R ₀ R ⁰ R ₀ R ⁰ R ₀ R ⁰	r ⁰ r ⁰ r ⁰ r ⁰ r ⁰ r ⁰	0.0000 0.0000 0.0000

Table 20

Reaction with anti-Le ^a	Reaction with anti-Le ^b	Phenotypes
+	—	Le(a+b—)
—	+	Le(a—b+)
—	—	Le(a—b—)
+	+	Le(a+b+)*

* In individuals of groups 0 and A₂.

The Lewis antigens are primarily substances present in the saliva and serum (GRUBB⁷⁹), and the erythrocytes obtain them by absorption from the latter (SNEATH and SNEATH⁸⁰). Since the Lewis phenotype depends on the secretor genotype, a nonsecretor (*se se*) inheriting the Lewis gene *Le* has blood of the Lewis phenotype Le(a+b—), while under the same circumstances the blood of a secretor (*Se se* or *Se Se*) will be Le(a—b+). The prominence of the Lewis phenotype is also affected by the ABO group of the blood. Thus the A₂ gene interferes with both the Le^b (ANDRESEN⁷⁷) and Le^a (CUTBUSH et al.⁸¹) antigens (cf. Table 20). The genetic relationships between the Lewis groups of the erythrocytes and the secretion of Lewis and ABH substances in the saliva have been studied by GRUBB⁷⁹ and by CEPPELLINI⁸²; their views are summarized in Table 21.

Table 21

Genotype	Antigens				on erythrocytes
	ABH	Le ^a	Le ^{bL}	Le ^{bH}	
<i>Se Se Le Le</i> <i>Se Se Le le</i> <i>Se se Le Le</i> <i>Se se Le le</i>	+	+	+	+	Le(a—b+)
<i>se se Le Le</i> <i>se se Le le</i>	—	+	—	—	Le(a+b—)
<i>Se Se le le</i> <i>Se se le le</i>	+	—	—	+	Le(a—b—)
<i>se se le le</i>	—	—	—	—	Le(a—b—)

The Duffy blood-group system (CUTBUSH et al., 1950⁸³)

The antibodies anti-Fy^a (CUTBUSH et al.⁸³) and anti-Fy^b (IKIN et al.⁸⁴) react respectively with the human erythrocyte antigens Fy^a and Fy^b. The latter are determined by a pair of allelic genes *Fy^a* and *Fy^b*. SANGER et al.⁸⁵ described the phenotype Fy(a—b—), of common occurrence among negroes as well as the Jewish population of the Yemen. The Duffy blood groups are summarized in Table 22.

Table 22

Reaction with anti-Fy ^a	Reaction with anti-Fy ^b	Phenotype	Genotype
+	—	Fy(a+b—)	<i>Fy^aFy^a</i>
+	+	Fy(a+b+)	<i>Fy^aFy^b</i>
—	+	Fy(a—b+)	<i>Fy^bFy^b</i>
—	—	Fy(a—b—)	<i>Fy⁰Fy⁰</i>

The Kidd blood-group system (ALLEN et al., 1951⁸⁶)

The antibodies anti-Jk^a (ALLEN et al.⁸⁶) and anti-Jk^b (PLAUT et al.⁸⁷) react respectively with the human erythrocyte antigens Jk^a and Jk^b, determined by the allelic genes *Jk^a* and *Jk^b*. In the Kidd groups individuals have likewise been found whose blood reacts neither with anti-Jk^a nor with anti-Jk^b, i.e., of phenotype Jk(a—b—). The serum of such persons may contain the antibody anti-Jk^aJk^b (PINKERTON et al.⁸⁸). The Kidd blood groups are summarized in Table 23.

Table 23

Reaction with anti-Jk ^a	Reaction with anti-Jk ^b	Phenotype	Genotype
+	—	Jk(a+b—)	<i>Jk^aJk^a</i>
+	+	Jk(a+b+)	<i>Jk^aJk^b</i>
—	+	Jk(a—b+)	<i>Jk^bJk^b</i>
—	—	Jk(a—b—)	<i>Jk⁰Jk⁰</i>

The Diego blood-group system (LAYRISSE et al., 1955⁸⁹)

Anti-Di^a, first found in Venezuela by LAYRISSE et al.⁸⁹, defines an antigen Di^a so far detected on the erythrocytes of mongoloid peoples, particularly the South American Indians. Anti-Di^b also been described (THOMPSON et al.⁹⁰).

The Auberger blood-group system (SALMON et al., 1961⁹¹)

The antibody anti-Au^a has been found only once (SALMON et al.). The antigen Au^a is equally common among whites and negroes.

The Dombrock blood-group system (SWANSON et al., 1964⁹²)

SWANSON et al.⁹² described the antibody anti-Do^a, reacting with a hitherto unknown erythrocyte antigen Do^a present in about one-third of the bloods tested.

The Ii blood-group system (WIENER et al., 1956⁹³)

Anti-I is formed by those individuals whose erythrocytes carry the very small quantities of the antigen I (WIENER et al.⁹³). Anti-I consists either of autoantibodies or of rare, naturally occurring iso-antibodies of cold type. Cord-blood erythrocytes react only weakly with anti-I; the normal antigenic reaction develops gradually and reaches the adult level at 18 months. Anti-I was discovered by MARSH and JENKINS⁹⁴. There are various degrees of prominence among I carriers. A distinction is also made between i₁ (rare among whites) and i₂ (rare among negroes). A connection between the I and i characters and the ABO blood groups is likely (TIPPERT et al.⁹⁵).

The Xg blood-group system (MANN et al., 1962⁹⁶)

The Xg blood group is of particular genetic interest as the only one so far known that is inherited through the X chromosome. The antibody Xg^a is very rare. The antigen Xg^a, located on the short arm of the X chromosome, has contributed greatly to new knowledge of the topography of this chromosome.

The Yt blood-group system (EATON et al., 1956⁹⁷)

An antibody reacting with 99.6% of English bloods was discovered by EATON et al.⁹⁷ and named by them anti-Yt^a. Anti-Yt^a, which reacts with about 8% of bloods, was described by GILES and METANAS⁹⁸.

Antigens of infrequent occurrence (private antigens)

Antibodies have repeatedly been found which react with antigens often confined to a single family. The genetic classification of the genes corresponding to these family antigens presents difficulty, and usually it is only possible to demonstrate their serological independence of the blood-group characters described above in this chapter and of other individual, private or family antigens. The hereditary character of most of these antigens has been established, namely Levay⁹⁹, Jobbins⁹⁹, Becker¹⁰⁰, Ven¹⁰¹, W¹⁰², Re¹⁰³, Rm¹⁰⁴, By¹⁰⁴, Chr¹⁰⁵, Sw¹⁰⁶, Good¹⁰⁷, Bi¹⁰⁸, Tr¹⁰⁹. In other cases, inheritance has not been proved, namely Stobo¹¹⁰, Ot¹¹¹, Ho¹¹², Price¹¹³ and the antigens of the Bennett, Goodspeed, Sturgeon and Donna groups¹¹⁴.

Widely distributed antigens (public antigens)

These are antigens whose absence from human erythrocytes is an extremely rare occurrence. Examples are Vel¹¹⁵, Ge¹¹⁶, Lan¹¹⁷ and Sm¹¹⁷.

Clinical significance of the blood groups

Blood-group specific antibodies may bring about haemolytic reactions during blood transfusions or be the cause of haemolytic disease of the newborn. The most important and most widely distributed of the blood-group specific antibodies and their role in the causation of the haemolytic transfusion reaction (HTR) and haemolytic disease of the newborn (HDN) are summarized in Table 24.

Table 24 Clinical importance of the blood-group specific antibodies (adapted from METAXAS¹¹⁸)

Blood group system	Antibody	HTR	HDN	Blood group system	Antibody	HTR	HDN
ABO... ..	anti-A anti-B anti-A ₁ anti-H	Yes Yes Very rare No	Yes Rare No No	Kell.....	anti-K anti-k anti-Kp ^a anti-Kp ^b anti-Js ^a	Yes Very rare No No Rare	Yes Very rare No Very rare No
MNSs... ..	anti-M anti-N anti-S anti-s anti-U (S+s)	Very rare No Very rare Very rare Very rare	Very rare No Rare Rare Very rare	Lewis... ..	anti-Le ^a anti-Le ^b anti-X (Le ^a + Le ^b)	Yes Rare Yes	No No No
P.....	anti-P ₁	Very rare	No	Duffy... ..	anti-Fy ^a anti-Fy ^b	Yes ?	Very rare No
Rh... ..	anti-D anti-C anti-c anti-C ⁺ anti-E anti-e	Yes Yes Yes Yes Yes Rare	Yes Rare Yes Rare Yes Very rare	Kidd... ..	anti-Jk ^a anti-Jk ^b anti-Jk ^a Jk ^b	Yes Rare Rare	Rare Very rare ?
Lutheran .	anti-Lu ^a anti-Lu ^b	No Yes	No Very rare	Diego .	anti-Di ^a	Yes	?
				Auberger ..	anti-Au ^a	?	?

Serum groups¹

Some serum proteins exhibit a genetically determined allotype that allows serum groups to be distinguished. Such proteins include the γ -globulins (Gm groups), the α_2 -globulins (haptoglobins and Gc groups), the lipoproteins (Ag, Lp and Ld groups), the transferrins and serum cholinesterase. Polymorphism occurs not only among the serum enzymes but also among those of the erythrocytes, such as acid phosphatase²⁶, phosphoglucomutase²⁷, esterases²⁸ and lactate dehydrogenase²⁹.

Gm serum groups (GRUBB and LAURELL²) (genetic factors of the immune globulins)

The Gm serum groups are determined by the Gm factors located on the H chain and the Inv factors located on the L chain of the immune globulins (see also page 581). The Gm and Inv factors can be detected by means of the agglutination-inhibition reaction with Rh-positive erythrocytes carrying incomplete anti-D antibodies. A further character of the immune globulins, located on the H chain of the γ_{2b} type and independent of the Gm and Inv factors, is detected by a serum known as anti-ISf. So far, 22 Gm and 3 Inv characters have been described. The most important Gm factors are Gm^a (GRUBB and LAURELL²), Gm^b (HARBOE³), Gm^x (HARBOE and LUNDEVALLE⁴) and Gm^t (GOLD et al.⁵). In 1965 a new nomenclature was proposed under which these Gm factors would become Gm(1), Gm(5), Gm(2) and Gm(4) respectively, while the original Inv(1) factor would be redesignated Inv(1).

Haptoglobin groups (SMITHIES⁶)

When the α_2 -globulins are separated electrophoretically in starch gel the haptoglobin bands show group-specific differences. These allow three Hp phenotypes to be distinguished, corresponding to three genotypes (Table 1).

Table 1

Phenotype	Genotype
Hp 1-1	<i>Hp¹/Hp¹</i>
Hp 2-1	<i>Hp¹/Hp²</i>
Hp 2-2	<i>Hp²/Hp²</i>

Haptoglobins are normally absent from the blood of the newborn. Ahaptoglobinaemia may also result from intravascular haemolysis. True ahaptoglobinaemia, a defect in the blood proteins, is extremely rare.

A few rare variants of the haptoglobin groups have been reported, such as Hp-Ca (GALATIUS-JENSEN⁷) and the Johnson type (GIBLETT⁸); the latter occurs in two different modifications (1 and 2).

Group-specific components (Gc groups) (HIRSCHFELD⁹)

By immunoelectrophoretic separation of the α_2 -globulins HIRSCHFELD⁹ was able to show that these proteins exhibited an allotype he designated Gc grouping. A rapidly migrating Gc-1-1 type is distinguished from an intermediate Gc-2-1 type and a slowly migrating Gc-2-2 type.

Corresponding to these phenotypes are three genotypes owing their existence to the autosomal genes *Gc¹* and *Gc²*: *Gc¹Gc¹*, *Gc¹Gc²* and *Gc²Gc²*. Very rare variants are *Gc^x* (HIRSCHFELD¹⁰), *Gc^r* (HIRSCHFELD¹¹) and *Gc^z* (HENNIG and HOPPE¹²).

Lipoprotein groups (Ag groups [ALLISON and BLUMBERG¹³]; Lp groups [BERG¹⁴])

In the complex class of lipoproteins a distinction is made between high-density lipoproteins and low-density lipoproteins (LDL).

The latter also show a genetically determined allotype: this demonstrated by means of precipitating immune sera. A precipitating anti-LSL antibody was found by ALLISON and BERG¹³ in the serum of a patient who had received a large of blood transfusions and named by them anti-Ag. Iso-pr with anti-Ag specificity were also found in the blood of women who had had at least four pregnancies (DÜRWARD et al.¹⁵). Variations have since been described in addition to the Ag(a)¹⁶, namely Ag(b)¹⁶, Ag(x)¹⁷, Ag(a₁)¹⁸ and Ag(z)¹⁸. Recently, BERG¹³ has proposed the designation Ld(a) for yet Ag specificity.

It has not proved possible to produce a heterospecific serum from animals, though by immunizing rabbits BERG obtained heterospecific anti-LDL sera reacting with a further antigen, Lp. The genetic independence of the Ag and Lp characters appears to have been confirmed¹⁹. Isoimmunization against factor has not yet been reported. An anti-Lp serum has also been produced from horses²⁰. Whereas the original anti-Lp serum defined the factor Lp(a), the heterospecific anti-Lp horse serum reacts with the factor Lp(x).

Transferrin groups (SMITHIES²¹)

The transferrin groups (Tf groups) are due to polymorphism of the iron-binding β_1 -globulin transferrin (siderophilin). Up to 10 types of transferrin distinguished by their different electrophoretic mobilities are known (SMITHIES and HILLER²², GIBLETT et al.²³). Each transferrin corresponds to an autosomal gene, of which an individual possesses a pair. Most members of the white race are homozygotic for the gene *Tf^e*.

Cholinesterase groups (LEHMANN and RYAN²⁴, KALOW and GENEST²⁵)

Group-specific differences in the activity of the serum cholinesterase give rise to the cholinesterase groups. Their interpretation is still obscure.

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Unless otherwise stated, the following data apply to the lumbar fluid of adults drawn from the spinal subarachnoid space between the 3rd and 4th lumbar vertebrae. As a result of variations in the secretory, transudatory and resorptive processes there are some

	Mean	95% range (extreme range in brackets)	<i>s</i>	Reference	Remarks
Physicochemical data					
Pressure (mm Hg)					
Children	-	(3.0-7.5)	-	5	Determined with the subject lying on his side. Measured values are affected by the position of the subject, by breathing and by the heart beat. The pressure is increased by inhalation of CO ₂ and by alkalosis, decreased by inhalation of O ₂ and hyperventilation? Quacknill ¹⁰ felt the pressure is increased on compression of both jugular veins and returns to normal as soon as the compression is released. If the pressure of the spinal fluid increases on compression of a single jugular vein, this indicates thrombosis of the lateral venous sinus on the opposite side.
Adults	-	(4.5-13.5)	-	6	
Volume (ml)					
Infants	-	(40-60)	-	6	In adults the volume is made up of about 35 ml in the ventricles, 25 ml in the subarachnoid space and the cisternae, and 75 ml in the spinal canal.
Young children	-	(60-100)	-	6	
Older children	-	(80-120)	-	6	
Adults ..	135	(100-160)	-	6	
Appearance					
					cent
Leucocyte count (per μl)					
New born (0-14 days)					
Lumbar fluid	7.5	(0-15)	-	6	Val
Adults					
(a) Lumbar fluid	1.1	0-5.3	-	9	"
(b) Cisternal fluid	0.9	0-3.6	-	9	
(c) Ventricular fluid	-	(0-1)	-	10	
Erythrocyte count (per μl)					
New born (0-14 days)	120	(0-675)	-	6	Exc ind: can
Specific gravity	1.0070	(1.0062-1.0082)	-	12	Val
Freezing-point depression (°C)	0.569	(0.540-0.603)	-	12	Val spec
Osmolality (mosm/kg H₂O)	306	-	-	12	
Refractive index	-	(1.33494-1.33510)	-	14	
Surface tension (20 °C, dyn cm⁻¹)	61.5	60.0-63.0	0.75	15	Mea
Relative viscosity (38 °C)	-	(1.020-1.027)	-	16	
Specific conductivity (18 °C, S cm⁻¹)	0.01190	-	-	17	
Dry substance (g/kg)	10.8	(8.5-17.0)	-	19	Val
pH value					
Cisternal fluid	7.349	7.327-7.371	0.021	18	

	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Remarks
anolamine (mg/l)	-	(0.5-1.5)	-	40	The spinal fluid contains more ethanolamine than the serum
atine (mg/l)	-	(4.6-18.7)	-	41	
atiline (mg/l)	-	(6-14)	-	41	
ea (mg/l)	250	(138-364)	-	42	Values from 106 subjects by the urease method. The urea concentration of the spinal fluid is about three-quarters of that of the serum ^{42, 43} . It is increased in diseases accompanied by nitrogen retention.
ic acid (mg/l)	-	(5-26)	-	8	
etylcholine (μg/l)	-	(<20)	-	44	
istamine (μg/l)	9.7	(2-30)	-	45	
rotonin (μg/l)	1.04	0.66-1.42	0.19	46	Values from 48 subjects by a biological method.
doxylsulphuric acid (mg/l)	1.0	0.6-1.4	0.2	47	Values from 50 subjects. Increased in renal insufficiency.
ilirubin (mg/l)					
Newborn	2.4	0.4-4.4	1.0	48	Values from 34 newborn infants with a bilirubin serum level of 67 mg/l. The bilirubin concentration of the spinal fluid rises with that of the serum (correlation coefficient 0.58 ⁴⁹). Most of the bilirubin in the spinal fluid is in the unconjugated form ^{48, 49} .
Adults	-	(<0.1)	-	48	
roteins (mg/l)					
children					
1) 1-5 days	700	(250-900)	-	51	
2) 5-8 months	204	156-252	24	5	
adults					
c) Lumbar fluid	244	156-333	44	52	
d) Lumbar fluid	313	123-503	95	53	
e) Cisternal fluid	218	127-310	46	52	
f) Cisternal fluid	183	97-269	43	53	
g) Ventricular fluid	171	0-369	99	52	
Mucoproteins (mg/l)	51	15-87	18	50	
Sulic acid (mg/l)	5.1	3.3-6.9	0.9	51	Determined in 15 samples by the thiobarbituric acid method. The spinal fluid contains no free sulic acid.
β-Lipoproteins (mg/l)	0.39	(0.10-0.62)	0.18	52	Values from 12 subjects.

Paper-electrophoretic protein fractions of spinal fluid (as percentages of the total protein)

	Num- ber	Prealbumin		Albumin		α ₁ -Globulins		α ₂ -Globulins		β Globulins		γ Globulins		Refer- ence
		Mean	<i>s</i>	Mean	<i>s</i>	Mean	<i>s</i>	Mean	<i>s</i>	Mean	<i>s</i>	Mean	<i>s</i>	
Children (1-5 days)	35	2.5		47.4		6.8		8.8		14.5		20.0		51
Adults														
Lumbar fluid	22	3.4	1.98	54.8	6.95	8.8	0.24	7.9	1.77	9.8 (5.8-13.3)*	1.71	9.8	2.88	52
Cisternal fluid	13	4.6	1.6	44.6	7.3	6.7	1.0	9.5	3.7	18.5	4.8	11.2	2.7	53
Ventricular fluid	7	6.3	1.8	46.4	6.5	8.1	1.7	7.9	2.8	21.3	4.5	13.4	4.0	53
										19.1	2.0	10.3	2.7	52

* Total β-fraction, first value β fraction, second value β₂ fraction.

	Mean	95% range (extreme range in brackets)	n	Refer- ence	Remarks
Carbohydrates and non-nitrogenous metabolites					
Glucose (mg/l)					
(a) Lumbar fluid	615	487-743	64	78	Determined by (a) glucose oxidase method, (b) Benedict's method
(b) Lumbar fluid	670	480-860	95	78	
(c) Lumbar fluid	-	(500-800)	-	10	
(c) Cisternal fluid	-	(500-900)	-	10	
(c) Ventricular fluid	-	(500-900)	-	10	
Fructose (mg/l)					
	34	(24-42)	-	77	
Glucosamine (mg/l)					
	90	(50-180)	-	78	
Inositol (mg/l)					
	25.5	13.7-37.3	59	78	Values from 14 subjects
Pyruvic acid (mg/l)					
	-	(4-7)	-	80	Diagnostic use of this assay has been suggested ⁸⁷
α-Ketoglutaric acid (mg/l)					
	-	(0.3-2.9)	-	80	
Oxaloacetic acid (mg/l)					
	-	(0.8-1.1)	-	80	
Succinic acid (mg/l)					
	-	(2.8-3.9)	-	82	
Citric acid (mg/l)					
Lumbar fluid	54	-	-	83	Values from 30-year old subjects. The citric acid concentration of the spinal fluid increases with age.
Cisternal fluid	37	-	-	83	
Lactic acid (mEq/l)					
	1.6	0.84-2.36	0.38	22	Values by an enzyme method from 23 subjects whose serum lactic acid level was 1.4 mEq/l.
Acetoacetic acid (mg/l)					
	2.67	(1.61-5.46)	1.26	88	Values by an enzyme method from 11 subjects
β-Hydroxybutyric acid (mg/l)					
	4.83	(2.47-9.80)	2.49	88	Values by an enzyme method from 11 subjects
Vitamins					
Thiamine (μg/l)					
(a)	-	(13-17)	-	84	Values from (a) 45 subjects with <i>Ochromonas malhamensis</i> , (b) 36 subjects with <i>Ochromonas danica</i> . In the spinal fluid thiamine occurs in both the free and phosphorylated form ⁸
(b)	4	(3-12)	-	85	
Vitamin B₆ (μg/l)					
	-	(0-0.75)	-	84	Determined with <i>Tetrahymena pyriformis</i>
Nicotinic acid (mg/l)					
	-	(0.1-0.5)	-	8	
Folic acid (μg/l)					
(a)	-	(10-30)	-	86	Determined with (a) <i>Lactobacillus casei</i> , (b) <i>Pedococcus cerevisiae</i> . For methods see page 478.
(b)	-	(1-5)	-	86	
Vitamin B₁₂ (ng/l)					
	-	(0-30)	-	86	Determined with <i>Ochromonas malhamensis</i>
Pantothenic acid (mg/l)					
	0.52	(0.10-1.7)	-	84	Values from 103 subjects determined with <i>Lactobacillus plantarum</i> . Present mainly in the combined form.
Ascorbic acid (mg/l)					
	-	(3-21)	-	8	Present in the reduced form.

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- ¹ Henssler and Gernerz in Lange et al. (Eds.) *Hoppe-Seyler'sche Handbuch der physiologischen und pathologischen chemischen Analyse*, vol. 5, Springer, Berlin, 1953, page 301.

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9
10

	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Remarks
Enzymes*	About 30 enzymes have so far been identified in the spinal fluid ^{4,6} . In ad- dition to those listed, the spinal fluid contains various esterases (e.g., cholinest- erases, ribonuclease, isocitrate dehydrogenase and succinate dehydrog- enase). There is no direct relationship between the enzyme activity of the seru- m and that of the spinal fluid. Disturbances of the permeability of the blood and blood-spinal fluid barriers may result in transudation of enzymes from serum and cerebral parenchyma into the spinal fluid.
1.1.1.14 L-Iditol dehydrogenase (U/l, 25 °C)	1.0	0.54–1.46	0.23	63	Values from children aged 2–15 years.
1.1.1.27 Lactate dehydrogenase (U/l, 25 °C)	18.4	6.8–30.0	5.8	64	The proportions of the individual isoenzymes in the spinal fluid are mu- ch the same as in the serum ⁶⁵ . No significant age differences have been obser- ved in children ⁶³ .
1.1.1.37 Malate dehydrogenase (U/l, 25 °C)	20.8	12.8–28.8	4.0	64	
2.1.3.3 Ornithine carbamoyltrans- ferase (U/l, 37 °C)	0.31	0.05–0.57	0.13	66	Values from 77 children.
2.6.1.1 Aspartate aminotransferase (U/l, 25 °C)	–	(0–10)	–	67	Determined spectrophotometrically. Significant age differences have not been observed in children ⁶³ .
2.6.1.2 Alanine aminotransferase (U/l, 25 °C)	–	(0–9)	–	67	
3.4.1.1 Leucine aminopeptidase (U/l, 37 °C)	0.17	(0.05–0.28)	–	68	
4.1.2.13 Fructose diphosphate aldolase (U/l, 37 °C)	0.29	0–0.73	0.22	64	
5.3.1.6 Ribose phosphate isomerase (U/l, 37 °C)	1.2	(0.5–1.3)	–	69	
5.3.1.9 Glucose phosphate isomerase (U/l, 37 °C)	15	(2.5–38)	–	69	
Lipids					
Total lipids (mg/l)	12.52	7.66–17.4	2.43	69	The spinal fluid contains triglycerides, phospholipids, cholesterol and ch- olesterol esters. The fatty acid composition of the spinal fluid lipids is qualitatively similar to that of the plasma lipids; the proportion of linoleic acid in the spi- nal fluid fatty acids (4%) is lower than that in the plasma fatty acids (24%) ⁷ .
Neutral fats (mg/l)	4.17	0–9.01	2.42	59	Calculated by difference. Probably consist mainly of triglycerides.
Cholesterol (mg/l)					
(a)	3.95	2.19–5.71	0.88	59	The proportion of free cholesterol was (a) 33%, (b) 44%.
(b)	4.63	1.55–7.71	1.54	71	
Phospholipids					
(mg/l)	5.49	2.09–8.89	1.70	71	The phospholipids of the spinal fluid consist of lecithins, cephalins, plasm- alogens, sphingomyelins and small amounts of lysocleithins ^{55,72} . In neu- rological diseases the phospholipid concentration of the spinal fluid is often increa- sed in diseases accompanied by breakdown of myelin in the nervous tissue cephalin concentration of the spinal fluid is increased ⁷³ .
(μmol/l)	5.21	3.41–7.01	0.90	59	
Total fatty acids (μmol/l) ...	70	42–98	14	74	

* Given are the numbers and trivial names recommended by the Enzyme Commission of the International Union of Biochemistry (see pages 385–386)
definition of the unit U see page 584.

	Mean	95% range (extreme range in brackets)	n	Refer- ence	Remarks
Carbohydrates and non-nitrogenous metabolites					
glucose (mg/l)					
Lumbar fluid	615	487-743	64	75	Determined by (a) glucose oxidase method, (b) FOTIN-WU method, (c) HAGEDORN-JENSEN method. Glucose can also be determined by the
Lumbar fluid	670	480-860	95	75	
Lumbar fluid	-	(500-800)	-	70	
Cisternal fluid	-	(500-900)	-	70	
Ventricular fluid	-	(500-900)	-	70	
fructose (mg/l)	34	(24-42)	-	77	
ucosamine (mg/l)	90	(50-180)	-	76	
ositol (mg/l)	25.5	13.7-37.3	59	79	Values from 14 subjects.
ruvic acid (mg/l)	-	(4-7)	-	60	Diagnostic use of this assay has been suggested ⁶⁷
Ketoglutaric acid (mg/l)	-	(0.3-2.9)	-	60	
aloacetic acid (mg/l)	-	(0.8-1.1)	-	60	
ecinic acid (mg/l)	-	(2.8-3.9)	-	62	
tric acid (mg/l)					
umbar fluid	54	-	-	63	Values from 30-year old subjects. The citric acid concentration of the spinal fluid increases with age.
sternal fluid	37	-	-	63	
ctic acid (mEq/l)	1.6	0.84-2.36	0.38	22	Values by an enzyme method from 23 subjects whose serum lactic acid level was 1.4 mEq/l.
etoacetic acid (mg/l)	2.67	(1.61-5.46)	1.26	66	Values by an enzyme method from 11 subjects.
Hydroxybutyric acid (mg/l)	4.83	(2.47-9.80)	2.49	66	Values by an enzyme method from 11 subjects.
Amines					
hiamine (μg/l)					
h)	-	(13-17)	-	64	Values from (a) 45 subjects with <i>Ochromonas malkinensis</i> , (b) 36 subjects with <i>Ochromonas danica</i> . In the spinal fluid thiamine occurs in both the free and phosphorylated form ⁶
h)	4	(3-12)	-	68	
hiamin B ₁₂ (μg/l)	-	(0-0.75)	-	64	Determined with <i>Tetrahymena pyriformis</i>
lcotinic acid (mg/l)	-	(0.1-0.5)	-	7	
olic acid (μg/l)					
h)	-	(10-30)	-	26	Determined with (a) <i>Lactobacillus casei</i> , (b) <i>Pedococcus cerevisiae</i> . For methods see page 478.
h)	-	(1-5)	-	26	
hiamin B ₁₂ (ng/l)	-	(0-30)	-	63	Determined with <i>Ochromonas malkinensis</i>
anthoic acid (mg/l)	0.52	(0.10-1.7)	-	66	Values from 103 subjects determined with <i>Lactobacillus plantarum</i> . Present mainly in the combined form.
scotic acid (mg/l)	-	(3-21)	-	7	Present in the reduced form.

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Synovial Fluid

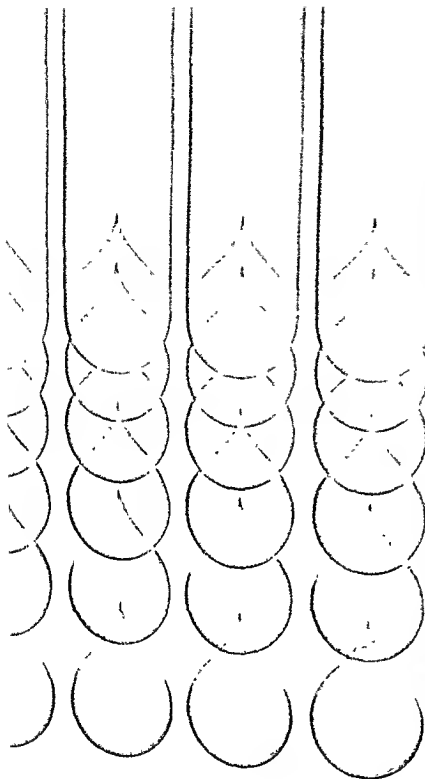
(For references see page 642)

The synovial fluid consists of a serum ultrafiltrate together with a secretion formed by the cells of the synovial membrane; the latter component contains mucopolysaccharides. Normal values for the synovial fluid have been assembled by ROPES and BAUER¹ and by

DITTMER². For changes in the composition of the synovial fluid in disease see the literature^{1, 3, 4}.

Unless otherwise stated, the data given below refer to synovial fluid from the knee joint.

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Physical data					
Volume (ml).....	1.1	(0.13–4.00)	—	2	Often increased to 10–30 ml in joint disease.
Specific gravity (20 °C/20 °C).....	—	(1.0081– 1.015)	—	5	Postmortem values in 25 subjects.
Viscosity					
Relative viscosity (37 °C)....	—	(>300)	—	6	The viscosity is dependent on the hyaluronic acid content. It is often diminished in joint disease ^{6, 7} .
Intrinsic viscosity (37 °C)....	46.3	26.9–65.7	9.7	6	
Cells (per µl).....	63	(13–180)	—	8	Consist of 63% mononuclear phagocytes, 25% lymphocytes, 6.5% morphonuclear leucocytes and 4% synovial cells; any erythrocytes not arise from injury during aspiration. The various kinds of cell present in fluid in rheumatic diseases have been studied ⁹ .
pH value.....	7.434	(7.31–7.64)	—	10	Measured in vivo. The pH is lower in inflammatory joint disease.
Water (g/kg).....	—	(960–988)	—	5	Postmortem values in 25 subjects.
Dry substance (g/kg).....	34	(12–48)	—	2	
Inorganic substances					
Carbon dioxide (mmol/l)...	—	(19.3–30.6)	—	11	In accordance with the DONNAN equilibrium the bicarbonate concentration of the synovial fluid is higher than that of the serum ¹ .
Chloride (mEq/l).....	107.4	(87–138)	—	7	In accordance with the DONNAN equilibrium the chloride concentration of the synovial fluid is higher than that of the serum ¹ .



marks

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ed in rheumatic degenerative arthritis and

idance with the DONNAN equilibrium the
sial fluid is lower than that of the serum¹. It
n joint disease?

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sial fluid is lower than that of the serum¹. It
joint disease?

accordance with the DONNAN equilibrium
sial fluid is lower than that of the serum¹.
Calcium pyrophosphate crystals have been

quilibrium the magnesium concentration of
it of the serum¹

s Increased in rheumatoid arthritis

d in rheumatoid arthritis

Increased in joint disease as a result of the

total nitrogen

synovial fluid is roughly equal to that of the
sre often found in the synovial fluid^{1, 6}.

ues in the literature, (b) determined in 6 men
rtion of albumin is higher than in the serum,
portion of α_2 -globulin is usually higher than
hapoglobin content is low²⁴ and fibrinogen
scent²⁵. The protein concentration is usually
22 26 42, especially in rheumatoid arthritis.
eoglobulin²⁴, γ globulin^{22 23 42} and caetulo-

re synovial fluid and include lactate dehydro-
ase^{28 29}, isocitrate dehydrogenase³⁰, glutar-
ninosyl transferase^{28 30}, alanine aminotransfer-
ase³¹, β glucuronidase³², aminopeptidase³³,
³⁴ and glucose phosphate isomerase^{28 30}
emes lie within or below their normal ranges
if many of them are increased in inflammatory

roton^{*}

Long-acting
diuretic

Smooth, continuous
control in edema

ultra	α_2 -Globulin/ α_2 globulin ratio	Ultracentrifuge			
		19S	7S	4S	1S
%		%	%	%	%
4	1.0	—	—	—	—
3	1.3	2	12	83	3
1	0.7	3	8	88	1
6	0.5	4	24	72	0
6	0.5	2	12	86	0

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The synovial fluid consists of a se
a secretion formed by the cells of the
component contains mucopolysaccl
synovial fluid have been assembled

Physical data

Volume (ml).....

Specific gravity
(20 °C/20 °C) ...

brings
inflammation
under control



	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Reducing substances (glucose)	The glucose concentration of the synovial fluid is about the same as that of serum in health but lower in inflammatory joint disease (see table below)
Hyaluronic acid (g/l)	3.21	2.45-3.97 (2.50-3.65)	0.38	34	Determined in 8 subjects as hexuronic acid. The hyaluronate normally contains 2% of protein ³⁵ , that from pathological effusions 10% ²⁶ . In joint disease the hyaluronate concentration is usually lowered ^{6,7,23,26,34} . The degree of polymerization of the hyaluronate is lowered in inflammatory joint disease; this results in a lowering of the intrinsic viscosity of the synovial fluid and is responsible for the pathological result in the mucin test (see table below).
Sialic acid (g/l)	0.28	0.14-0.42	0.07	37	Determined in 10 samples by the diphenylamine reaction.
Lactic acid	The lactic acid concentration of the synovial fluid is the same as that of serum but is increased in inflammatory joint disease ^{7,38} .
Ascorbic acid (mg/l)	-	(1.5-11.6)	-	39	Measured in 6 patients with rheumatoid arthritis.
Lipids	In joint disease the lipid concentration of the synovial fluid is about 10 times greater than normal ^{40,41} .
Cholesterol (mg/l)	71	-	-	41	
	-	(50-140)	-	21	
Phospholipids (mg/l)	138	(130-150)	-	41	
Triglycerides (mg/l)	0	-	-	41	

Synovial fluid in joint disease⁴

	Normal	Noninflammatory	Inflammatory	Septic	Haemorrhagic
Volume (ml)	<3.5	>3.5	>3.5	>3.5	>3.5
Appearance	clear, colourless	straw-yellow, clear	cloudy, yellow	cloudy, yellow	bloody
Viscosity	high	high	low	low	variable
Fibrin clot	absent	usually absent	present	present	usually absent
Mucin clot*	strong	strong	friable	friable	variable
Nucleate cells per microlitre	<200	200-5000	2000-100 000	20 000-200 000	200-10 000
Polymorphonuclear leucocytes in nucleate cells (%)	<25	<25	>50	>75	<50
Difference between glucose contents of blood and synovial fluid (mg/l)	<100	<100	>250	>250	<250
Cultures	negative	negative	negative	often positive	negative

* After addition of acetic acid.

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	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Phosphorus (mg/l)					
Parotid saliva					
(a) Inorganic phosphorus ...	201	14-388 (90-420)	93.5	⁹	Values from (a) 42, (b) 28, (c) 120, (d) 50, (e) 180 subjects. The inorganic phosphate content falls with increasing rate of secretion ² . Most of the organic phosphorus is acid-soluble and contains phosphoethanolamine ²¹ as well as adenosine phosphates, sugar phosphates and phosphoglyceric acid ²² ; the acid-insoluble fraction contains traces of phospholipids ²⁰ .
Submandibular saliva					
(b) Inorganic phosphorus ...	148	26-270 (70-350)	61	⁹	
Total saliva					
(c) Total phosphorus	204	120-288	42	²⁰	
(d) Organic phosphorus	55	0-133	39	²⁰	
(e) Inorganic phosphorus ...	149	81-217	34	²⁰	
Sulphur (mg/l)	-	(30-200)	-	²³	Values from 5 subjects. Most of the sulphur is probably present in the form of thiocyanate.
Bromide (mg/l)	-	(0.2-7.1)	-	²⁴	
Fluoride (mg/l)	-	(0.08-0.25)	-	⁴	The fluoride content of saliva appears to be independent of that of the drinking water.
Iodide (mg/l)	0.102	0.002-0.202 (0.035-0.240)	0.05	²⁵	In men most of the iodine present in saliva is in the form of iodide ²⁶ . The iodine content of the saliva is 7-100 times higher than that of the serum; iodine concentration occurs in the parotid and submandibular glands but not in the sublingual glands ²⁶ . The highest iodide concentration is associated with low rates of secretion ^{27,28} . The relationship between iodine concentration in the saliva and thyroid function has been studied ²⁹ .
Thiocyanate (mg/l)	113	0-257 (24-380)	72	³⁰	Values from 37 nonsmokers; mean value in smokers 321 mg/l. Like iodide thiocyanate is preferentially secreted by the salivary glands. The thiocyanate content of parotid saliva falls with increasing rate of secretion ²⁷ .
Potassium (mEq/l)					
(a) Parotid saliva	25.1	11.7-38.5 (15-46)	6.7	⁹	Values from (a) 42, (b) 28, (c) 4 and (d) 9 subjects; values (e) are from children and adults. In all salivary fractions the potassium content is higher than in the serum. In young children the potassium content is higher than in adults ³² , in whom it is largely independent of age and sex ³³ . At rates of secretion over 0.5 ml/min the potassium content is roughly constant, at rates below this figure increased ^{37,31,34-36} . The literature contains conflicting data on hourly fluctuations ^{9,31,33,37} .
(b) Submandibular saliva	18.0	6.8-29.2 (10-38)	5.6	⁹	
(c) Sublingual saliva	-	(18-40)	-	⁹	
Total saliva					
(d) Resting saliva	20.7	(14-41)	-	⁹	
(e) At a minute volume of 2 ml	19	11-27	4	³¹	
Sodium (mEq/l)					
(a) Parotid saliva	6.9	0-15.9 (1.7-17)	4.5	⁹	Values from (a) 42, (b) 28, (c) 4 and (d) 9 subjects; values (e) are from children and adults. In all salivary fractions the sodium content is less than that of the serum and rises with increasing rate of secretion ^{2,17,31,34,35} . In young children, the sodium content is higher than in adults ³² , in whom it is largely independent of age and sex ³³ . The literature contains conflicting data on hourly fluctuations ^{9,31,33,37} . In children with cystic pancreatic fibrosis the sodium content of the saliva shows a significant increase ³⁸ .
(b) Submandibular saliva	5.1	0.3-9.9 (0.9-10)	2.4	⁹	
(c) Sublingual saliva	-	(11-120)	-	⁹	
Total saliva					
(d) Resting saliva	14.4	(5.2-24.4)	-	⁹	
(e) At a minute volume of 2 ml	24	12-36	6	³¹	
Sodium-potassium ratio					
(a) Resting saliva	0.7	-	-	-	(a) Calculated from the sodium and potassium contents of the total saliva; (b) applies to children and adults. Since the potassium content of saliva is largely independent of the rate of secretion whereas the sodium content is proportional to the latter the sodium-potassium ratio necessarily rises with increasing rate of secretion. The sodium and potassium contents of saliva are related to the functioning of the anterior pituitary-adrenocortical system; during treatment with deoxycorticosterone the ratio falls as a result of sodium retention ³⁹ , and it is also reduced in primary aldosteronism ⁴⁰ .
(b) At a minute volume of 2 ml	1.35	0.6-2.1	0.375	³¹	
Calcium (mEq/l)					
Parotid saliva	1.5	-	-	⁴¹	The calcium content, especially that of the submandibular saliva, rises with increasing rate of secretion ^{2,42} . An increased calcium content of the submandibular saliva has been observed in cystic pancreatic fibrosis ⁴³ .
Submandibular saliva	-	(3-6)	-	³	
Total saliva	3.1	(2.3-5.5)	-	⁶	

	Mean	95% range (extreme range in brackets)	<i>n</i>	Refer- ence	Remarks
Magnesium (mEq/l)					
Parotid saliva	0.6	-	-	2	
Submandibular saliva	0.6	-	-	2	
Total saliva	0.6	(0.16-1.06)	-	6	
Cobalt ($\mu\text{g/l}$)	-	(0-125)	-	44	Values from the stimulated saliva of 7 subjects, cobalt could be detected in only 10 out of 37 saliva specimens.
Copper ($\mu\text{g/l}$)	317	(50-760)	151	48	Values from 30 subjects
Nitrogenous constituents					
Total nitrogen (g/l)					
(a) Parotid saliva	0.586	0.140-1.032	0.223	2	
(b) Submandibular saliva	0.268	0.102-0.434	0.083	2	
(c) Total saliva	0.60	(0.20-1.07)	-	2	
Urea (mg/l)					
Parotid saliva	252	-	-	41	The urea content of saliva is usually 75-90% of the content in the blood
Total saliva	200	(140-750)	-	4	
Creatinine (mg/l)	-	(5-20)	-	4	Values depend on the method used ²¹
Ammonia (mg/l)	60	(10-120)	-	6	Values from stimulated saliva. The wide fluctuation in the ammonia content is partly explained by the instability of urea.
Amino acids					
Choline (mg/l)	-	(5-36)	-	42	Measured on stimulated saliva in 2 subjects. Phosphoethanolamine has also been found in parotid and submandibular saliva ²¹
Uric acid (mg/l)	15	(5-29)	-	2	The uric acid content is higher in stimulated saliva
Histamine (mg/l)	0.15	(0.11-0.18)	-	20	Measured in 48 samples from 24 healthy subjects. There are no considerable fluctuations during the course of the day
Proteins (g/l)					
(a) Parotid saliva	2.62	0.5-3.8	1.38	22	(a) Values from 25 subjects by the biuret reaction, (b) range of values in the literature. The salivary proteins consist mainly of mucins, plasma proteins and enzymes, they arise in part from bacteria, epithelial cells and leucocytes. The protein content of parotid saliva is constant at rates of secretion exceeding 0.1 ml/min but reduced at lower rates of secretion ²⁴ . Various plasma proteins have been detected in saliva by the immunoelectrophoretic technique ²²⁻²⁷ and include albumin, haemoglobin, transferrin, orosomucoid, γ A globulin and enzymes.
(b) Total saliva	-	(1.4-6.4)	-	4	
Mucins (g/l)	2.7	(0.8-6.0)	-	6	
Parotid saliva (mg/l)					
Hexosamine, bound	99	(20-223)	59	20	Measured on 26 subjects, aged 5-18 years
Fucose, bound	89	(33-244)	54	20	
Hexose, bound	195	(73-441)	100	20	
Sulphic acid, bound	12.4	(3.5-21.1)	81	20	
Enzymes					
Lysozyme (g/l)	-	up to 0.15	-	-	Enzymes should be looked for only in clean catheterized saliva since the total salivary enzyme content is very low.

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Amylase (ptyalin) (mg/ml)					
Parotid saliva	1.03	—	0.44	65	Values from 16 subjects. The amylase of saliva is an α -amylase; in parotid it is the main protein component ² . The amylase content depends on the of the stimulant ^{2, 66} . It is low in the newborn and reaches the adult va wards the end of the first year of life ² .
Submandibular saliva	0.25	—	0.24	65	
Sublingual saliva	0.26	—	0.32	65	
Total saliva	0.38	—	0.32	65	
Nitrogen-free substances					
Reducing substances (glucose) (mg/l)					
(a) Parotid saliva	11.4	—	—	41	(a) Measured by the HAGEORN-JENSEN method; (b) values from 39 su by the glucose oxidase method, (c) usual values in the literature bas reduction methods; values depend on the method used ⁶⁸ . Sex difference: not been observed; the glucose content of saliva is slightly increased i age ⁶⁷ . In addition to glucose, saliva contains maltose, arabinose and ribc
(b) Total saliva	26	2-50	12	67	
(c) Total saliva	—	(100-300)	—	4	
Citric acid (mg/l)	—	(up to 20)	—	4	Values from a variety of stimulated samples. When samples are allow stand for long the citric acid is broken down by bacteria.
Lactic acid (mg/l)	—	(10-50)	—	6	Values from stimulated saliva. The lactic acid content rises steeply after r Most of the lactic acid is a breakdown product of carbohydrates and m due to bacterial action.
Cholesterol (mg/l)	—	(25-500)	—	4	Cholesterol has been found in parotid and submandibular saliva ⁹ .
Vitamins					
Folic acid (μ g/l)	41	(2-165)	—	69	Determined with <i>Lactobacillus casei</i> in 24 subjects.
Ascorbic acid (mg/l)	2.18	0.58-3.78	0.80	70	Values from 31 healthy subjects. No connection has been demonstrated tween caries and the ascorbic acid content of the saliva.

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(For references see pages 650-651)

ing to the difficulty of collecting pure gastric juice the exact position of this body fluid is not known for certain. The use of gastric tube or even a gastric fistula yields not pure gastric but simply the gastric contents, almost always containing food remnants and occasionally also bile, pancreatic juice, intestinal contents. Unless otherwise stated, the following apply to unstimulated gastric juice obtained from fasting subjects by means of permanent intubation.

other cells (nonparietal secretion)^{1, 2}. Both these components are roughly isotonic with the serum. The volumes of the two components are related as follows:

$$V_p = V_{\text{total}} (0.219 + 4.88 A)$$

$$V_{np} = V_{\text{total}} - V_p$$

(V_{total} = total secretion [ml]; V_p = parietal secretion [ml], V_{np} = nonparietal secretion [ml], A = acidity [mEq/ml].)

The composition of the gastric juice thus depends on the proportions of the individual cellular secretions, the amounts and compositions of which are in turn dependent on the nature of the stimulus. There is a considerable literature on the composition of the gastric juice³⁻⁶, on the diagnostic aspects of gastric juice analysis see the literature^{7, 8}.

	Mean	95% range (extreme range in brackets)	<i>n</i>	Refer- ence	Remarks
biochemical data					
Volume (ml)					
Newborn...	2.65	(0.4-12.3)	205	9	
Infants...	2.4	(1.0-3.5)	97	10	
Children	8.8	(0.4-80)	82	10	
Adults	50	(0-180)	-	6	
Secretion					
Secretion rate (ml/h)					
Infants	18.6	(6-54)	18	10	
Young children					
Fasting (basal)	31	(10-64)	-	27	
After histamine (maximal)	52	(28-105)	-	27	
Children	50.4	(6-180)	252	10	
Adults					
Fasting (basal)	74	(0-176)	-	6	
At night	46	(12-99)	-	6	
After meals	101	(13-217)	-	6	
After histamine	117	(2-256)	-	6	
After insulin	124	(70-204)	-	6	
Specific gravity	-	(1.004-1.010)	-	6	
Freezing-point depression (°C)	0.47	(0.30-0.82)	-	6	
Viscosity (g/l)	-	(994-995)	-	3	
Trypsin substance (g/l)	5.6	-	-	3	
pH value					
1) Newborn	2.52	(1.2-7.4)	153	9	
2) Children	3.27	(0.9-7.7)	201	10	
3) Men	1.92	-	128	11	
4) Women	2.59	-	208	11	

	Mean	Extreme range	s	Reference	Remarks	
Acidity						
Total acid (mEq/l)						
(b) Children.....	38.2	(4-126)	21.6	10	Values from (a) 154 newborn children, (b) 695 samples from 59 (mean age 9 years), (c) 15 men and 4 women (aged 20-25), (d) 10 (mean age 21 months). The acid secreted by the parietal cells consists of hydrochloric acid, which is partly neutralized, buffered and diluted secretion of the other cells. The total acid corresponds to a titration of pH 7-8, the free acid to one of pH 2.5-3.5. The difference between total and free acid is known as bound acid and corresponds roughly to the part of the hydrochloric acid; whether this distinction is a valid one, is doubtful. The present preferred method is to titrate the acid to the point using phenol red or the electrometric technique up to pH 7.4 ² ; earlier 'clinical unit' was mEq acid per litre, corresponding to ml 0.1-NaOH per 100 ml.	
(c) Adults	-	(5-118)	-	14		
Free acid (mEq/l)						
(a) Newborn	21.4	-	11.7	9		
(b) Children.....	28.1	(0-100)	17.9	10		
(c) Adults	-	(0-115)	-	14		
Free acid (mEq/h)						
(d) Young children						
Fasting (basal)	0.48	(0.00-1.32)	-	27		
After histamine (maximal)	2.59	(0.80-3.73)	-	27		
(e) Men						
Fasting (basal)	2.4	-	-	8		
At night.....	1.7	-	-	8		
After betazol (submaximal)	11.6	-	-	8		
After histamine (submaximal)	11.8	-	-	8		
After histamine (maximal)	22.4	-	-	8		
After insulin	16.5	-	-	8		

Gastric juice secretion under maximal histamine stimulation (augmented histamine test). The acid secretion is determined both under basal conditions and following a subcutaneous dose of 0.04 mg histamine monophosphate per kilogramme body weight^{22,29,69}. The following are measured (all in mEq acid per unit of time):

- one-hour morning basal acid output (MBAO or BAO) = acid secretion during one hour in the morning without stimulation
- maximum acid output (MAO) or maximal secretory response (MSR) = acid secretion during one hour after maximum stimulation with histamine
- maximal histamine response (MHR) = acid secretion during the second and third quarter-hours after maximum stimulation with histamine
- peak acid output (PAO) = 2 × MHR

The acid secretion can also be stimulated²⁹ by betazol given subcutaneously (values for submaximal stimulation are given in the table below), by histamine given by the continuous intravenous route, by insulin or 2-deoxy-D-glucose (under vagus stimulation), or by gastrin or another synthetic pentapeptide of this type.

The acidity of both unstimulated and stimulated gastric juice varies with day and sex (see the tables below). The basal acid secretion varies with the day and is least at about 2 a.m.⁷⁷. The highest acidity values found in around 150 mEq/l²⁷. At birth the acid content of the gastric juice is¹⁸ but rises to the value given in the table during the first hours of life¹⁸ and there is good correlation between the acid secretion under histamine stimulation and body weight (about 2 mEq/h per 10 kg body weight)²⁷ maximum acid output is largely constant in any one individual and per measure of the total parietal cell mass³⁰; about 40 million parietal cells necessary to produce 1 mEq of hydrochloric acid per hour under maximum stimulation.

There has been much discussion of the usefulness of the acid secretion for the diagnosis of gastric and intestinal ulcers^{25,27}. If the basal acid exceeds 60% of the maximum acid output the patient is almost certainly suffering from the ZOLLINGER-ELLISON syndrome²². An acidity (pH) under maximum stimulation with histamine is rare³² and seen only in atrophy of the gastric mucosa, as for instance in pernicious anaemia.

Acid secretion in adults before and after maximum histamine stimulation (subcutaneous dose of 0.04 mg histamine monophosphate per kilogramme body weight)

	Number of subjects	Volume (ml/h)		Total acid (mEq/h)		Free acid (mEq/h)	
		mean	s	mean	s	mean	s
From DOTEVALL ⁷⁷							
Basal secretion							
Men.....	30	64.0	21.4	3.70*	2.12	2.59	1.97
Women.....	12	54.2	24.2	2.24*	1.76	1.48	1.33
After histamine							
Men.....	24	201.6	53.4	23.3**	6.9	20.5	6.8
Women.....	12	153.7	33.3	17.7**	5.4	15.7	5.1
From BARON ⁶⁹							
Basal secretion							
Men.....	20	38.7	23.01	1.3*	1.59	-	-
Women.....	20	40.6	38.8	1.1*	1.75	-	-
After histamine							
Men.....	20	177	73.3	17.1**	11.94	-	-
Women.....	20	107	57.7	9.4**	7.20	-	-

* Basal acid output (BAO). ** Maximal acid output (MAO).

* Basal acid output (BAO). ** Maximal acid output (MAO).

Acid secretion in adults before and after betazol stimulation⁷⁰ (subcutaneous dose of 0.5 mg betazol hydrochloride per kilogramme weight)

Age	Men					Women		
	Number	Free acid (mEq/h)			Number	Free acid (mEq/h)		
		Extreme range	Mean	s		Extreme range	Mean	
<i>Basal secretion</i>								
20-29 ...	74	0-17.1	2.50	2.81	65	0- 8.6	1.74	
30-39 ...	157	0-14.9	2.63	2.70	145	0-15.0	1.58	
40-49 ...	156	0-12.3	2.83	3.01	184	0-13.5	1.43	
50-59 ...	158	0-17.0	2.25	3.04	162	0- 6.7	0.98	
> 60....	70	0- 9.9	1.48	2.18	78	0- 7.6	0.95	
All ages .	615	0-17.1	2.44	2.85	634	0-15.0	1.33	
<i>After betazol</i>								
20-29 ...	74	0-29.6	11.46	6.69	65	0.3-20.8	7.79	
30-39 ...	157	0-31.3	12.83	6.69	145	0-22.1	7.83	
40-49 ...	156	0-48.4	13.29	8.66	184	0-24.7	8.12	
50-59 ...	158	0-31.5	10.67	7.11	162	0-22.8	6.90	
> 60....	70	0-24.8	7.67	7.56	78	0-20.0	6.67	
All ages .	615	0-48.4	11.64	7.62	634	0-24.7	7.53	

Gastric Juice

	Mean	95% range (extreme range in brackets)	Reference	Remarks
anionic substances				
bicarbonate	The secretion of the parietal cells is reported to contain 45 mEq bicarbonate ³⁷
chloride (mEq/l)	-	(77.6-159)	-	³⁸ The chloride content of the parietal secretion is about 170 mEq/l, if nonparietal secretion about 125 mEq/l ³⁷ . Values below 130 mEq/l contamination of the gastric juice by saliva and intestinal contents ³⁸
phosphorus (mg/l)	70	(66-180)	-	³⁹
sulfide (mg/l)	-	(0.6-9.0)	-	³⁹
sulfide (mg/l)	-	(0.4-0.7)	-	³⁹
thiocyanate	The presence of thiocyanate in the gastric juice indicates probable contamination with saliva ³⁸
potassium (mEq/l) ..	11.6	(6.4-16.6)	-	³⁷ Values from 50 men. Potassium is secreted in about the same concentration by the parietal cells as by the other cells. Changes in the potassium concentration with histamine stimulation are variable ³⁹ . High values indicate contamination with saliva
calcium (mEq/l)	49	(18.7-69.5)	-	³⁷
calcium (mEq/l)	3.6	(2.0-4.8)	-	³⁷ Values from 50 men. The calcium is found in the parietal secretion. Calcium values indicate contamination by saliva
magnesium (mEq/l)	1.5	(0.3-3.0)	-	³⁹ Values from 43 subjects
zinc (mg/l)	-	(0.1-0.4)	-	⁴⁰ Values from 7 subjects
nitrogenous substances				
total nitrogen (mg/l)	152	-	-	⁴¹ Values from (a) 21 patients with healthy stomachs, (b) 6 young men
	-	(10-2180)	-	⁴²
nonprotein nitrogen (mg/l)	415	-	-	⁴¹ Values from (a) 21 patients with healthy stomachs, (b) 10 subjects
	-	(150-320)	-	⁴² protein nitrogen represents about 20-30% of the total nitrogen
nitride nitrogen (mg/l)	-	(38-70)	-	⁴² Values from 10 subjects
amino-acid nitrogen (mg/l)	-	(16-75)	-	⁴² Values from 10 subjects
free amino acids (mg/l)	316	-	-	⁴³ Values from 15 subjects, 18 amino acids were determined. Hypocretin juice has an increased content of free amino acids. For a review see literature ⁴⁴
ammonia (mg/l)	97	67-127	15	⁴⁵ Values from 24 subjects. The ammonia content is increased in uremic states ⁴⁶ .
urea (mg/l)	84	-	15	⁴⁵ Values from 24 subjects. The urea content is increased in uremia.
histamine (mg/l)	-	(12-33)	-	⁴⁷
lactic acid (mg/l)	...	-	-	⁴⁸ (8-69)

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Histamine (µg/l)	—	(7–48)	—	47	
Proteins (g/l)	2.8	2.2–3.4	0.3	48	Determined by the biuret reaction; values in agreement with those obtained by other methods ^{46, 49, 50} .
Albumin (g/24 h)	—	(0.02–0.69)	—	51	The proteins of gastric juice are a very heterogeneous mixture ^{52, 53} and mucins rich in carbohydrate, enzymes and plasma proteins (albumin, γ-globulin, γA-globulin and others ⁵⁴). At low pH values they are readily broken down by enzymes into peptides and amino acids. Increased albumin occurs often in cancer of the stomach, in atrophic gastritis and also in MENÉTRIÉ's disease ^{52, 55} . On the rate of flow of plasma into the stomach WETTERFORS ⁵⁵ .
γ-Globulin (g/24 h)	—	(0.03–0.38)	—	51	
Mucins (g/l)	—	(0.6–15.0)	—	6	The mucins are contained in the covering-cell secretion (visible mucus) and are also secreted by the other cells of the glands except the parietal cells (mucopolysaccharides, mucoproteoses). The mucous substances are very heterogeneous ^{52, 53, 56, 57} and consist mainly of mucoproteins, sialic acid and mucopolysaccharides rich in fucose (including the blood-specific substances). The intrinsic factor (see page 484) and various vitamin B ₁₂ -binding substances are also mucoproteins. Determination of the intrinsic factor secretion is a diagnostic aid in pernicious anaemia ⁵⁸ .
Undissolved substances	1.4	—	—	56	
Trichloroacetic acid precipitate	1.0	—	—	56	
Mucoproteins	0.5	—	—	56	
Mucoproteoses	1.2	—	—	56	
Carbohydrates, bound (mg/l)					
(a) Hexoses	321	—	—	50	Values from (a) 16, (b) 10, (c) 15, (d) 13 and (e) 12 subjects. The carbohydrates are components of the mucoproteins and mucopolysaccharides. Their distribution has been studied by electrophoretic separation of the protein fractions. An increase in the carbohydrate content of the gastric juice has been observed in cancer of the stomach and pernicious anaemia ⁵⁰ .
(b) Hexosamines	327	—	—	50	
(c) Fucose	138	—	—	50	
(d) Sialic acid	73	—	—	50	
(e) Glucuronic acid	20	—	—	50	
Lactic acid	Lactic acid arises from the carbohydrates by bacterial action, but only in acid and hypoaacid gastric juice.
Lipids	The gastric juice appears to contain small amounts of lipids ⁶⁰ but these have not been further investigated.
Enzymes	The gastric juice contains mainly protein-splitting enzymes ⁵² . Other enzymes present are lipase ⁶¹ , lysozyme ⁶² , lactate dehydrogenase ^{63, 64} , isocitrate dehydrogenase ⁶⁴ , aminotransferases ⁶⁴ , fructose diphosphate aldolase ⁶⁴ , alkaline phosphatase ⁶⁴ , leucine aminopeptidase ⁶⁴ , oxoglutarate dehydrogenase ⁶⁴ , coenzyme phosphate isomerase ⁶⁴ , β-glucuronidase ⁶⁴ and ribonuclease ⁶⁴ ; the last ⁶⁶ is probably of bacterial origin. The lactate dehydrogenase and β-glucuronidase contents are increased in cancer of the stomach.
Pepsin (kU/24 h, 37 °C)					
Men	28.8	—	13.5	65	Values from 10 men and 10 women (for definition of the unit U see page 1). The gastric juice in man contains at least 3 protein-splitting enzymes ⁵² , namely 2 pepsins and a protease with a maximum activity at pH 7. According to TAYLOR ⁶⁶ one pepsin is secreted by the chief cells of the fundus glands and the other by the pylorus glands. According to TANG and WOLF ⁶⁷ the proteolytic activity at pH 2 is due to the pepsins, that at pH 3.5 to gastricsin. The peptic content of the gastric juice is greatly reduced after histamine stimulation and greatly increased after vagus stimulation; it is decreased in cancer of the stomach and atrophy of the gastric mucosa ^{12, 68} .
Women	18.9	—	7.5	65	
Vitamins					
Vitamin B ₁₂ (µg/l)	—	(0.06–3.0)	—	68	
Ascorbic acid (mg/l)	—	(1.5–15.0)	—	5	

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Pancreatic Juice

(For references see page 653)

The pancreatic juice probably arises from two different types of cells: the one type, presumably the epithelial cells of the ducts, secrete a very watery juice rich in bicarbonate, whereas the other type, the epithelial cells of the acini, produce a viscous secretion rich in enzymes. Various stimuli, for instance acids, bring about the liberation of secretin and pancreaticozym from the duodenal mucosa. Secretin stimulates mainly the secretion of fluid and bicar-

bonate, while pancreaticozym, acetylcholine and vagus stimulation cause an increase in the liberation of enzymes. Unless otherwise stated, the data given in the table below apply to unstimulated pancreatic juice obtained either by means of intubation (here designated duodenal contents) or an external pancreatic fistula. For further data on the pancreatic juice see the literature¹⁻³

	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Remarks
Physicochemical data					
Appearance					Watery, colourless, thin fluid, clear or slightly opalescent. Because of its similarity to saliva, the pancreatic juice is also known as abdominal saliva.
Secretion rate (ml/h)					
Young children	-	(4-13)	-	4	
Adults	36	(>0-99)	-	2	
Secretin test ⁴⁻⁵					
(ml/h)	176	38-314	69	9	Value
(ml/h/kg body weight)	2.68	1.04-4.32	0.82	9	"
					"
Specific gravity	-	(1.008-1.011)	-	11-12	
Freezing-point depression (°C)	-	(0.55-0.63)	-	12, 13	The
Water (g/l)	987	-	-	11	
Dry substance (g/l)	13.0	(7.5-15.7)	-	14	Value
pH value	-	(7.5-8.8)	-	15, 16	

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Inorganic substances					
Bicarbonate (mEq/l).....	-	(25-[150])	-	17	The bicarbonate content of pancreatic juice rises in the form of a hyperbolic curve from 25 mEq/l at a secretory rate of 40 ml/h up to 130-150 mEq/l at secretory rate of 300 ml/h. The sum of the bicarbonate and chloride concentrations is constant and amounts to about 154 mEq/kg water ¹⁷ .
Secretin test ¹⁻³					
(mEq/l).....	13.5	0-27.1	6.8	9	Values from 47 adults with a healthy pancreas, obtained by analysing the pancreatic juice during the hour following intravenous injection of 2 units secretin per kilogramme body weight. The results of the test in adults are almost independent of sex and age ¹⁰ . The bicarbonate concentration is decreased in chronic pancreatitis.
(mEq/kg body weight) ...	0.199	0.047-0.351	0.076	9	
(mEq/l).....	76	62-90	7	9	
Chloride (mEq/l).....	-	([4]-129)	-	17	The chloride content of pancreatic juice is determined by the bicarbonate content (see under 'Bicarbonate' above). With increasing secretory rate the chloride content falls in the form of a hyperbolic curve.
Phosphate (mmol/kg water)	0.8	0-1.6	0.4	17	From analysis of the duodenal contents. The values accord with those for fistular juice ¹⁶ .
Potassium (mEq/l)	-	(6-9)	-	17	In (a) duodenal contents, (b) fistular juice.
(a).....	-	(4.1-5.5)	-	16	
(b).....	-	(139-143)	-	17	From analysis of the duodenal contents; in agreement with values from the fistular juice of 3 subjects ¹⁵ . The sodium content of the pancreatic juice largely parallels that of the serum.
Sodium (mEq/l).....	-	(139-143)	-	17	
Calcium (mEq/kg water)...	3.4	2.2-4.6	0.6	17	From analysis of the duodenal contents; in agreement with values from the fistular juice of 3 subjects ¹⁵ .
Magnesium (mEq/kg water)	1.0	-	-	17	From analysis of the duodenal contents.
Other minerals.....	The following have also been found in the fistular juice ¹ : sulphur (but no sulphate ¹⁵), silicic acid, zinc (a component of carboxypeptidase A) and traces of copper.
Organic substances					
Total nitrogen (g/l).....	-	(0.76-0.98)	-	1	Results of analyses of fistular juice made during the period 1902-1912.
Nonprotein nitrogen (g/l) ..	0.14	-	-	15	From the fistular juice in 3 subjects.
Proteins (g/l)	-	(4.8-5.3)	-	18	Values from (a) duodenal contents of 3 subjects, (b) fistular juice of 3 subjects.
(a).....	-	(1.9-3.4)	-	15	The greater part of the proteins in pancreatic juice are enzymes and their precursors, the remainder plasma- and mucoproteins. Electrophoretic separation has yielded up to 7 fractions ¹⁴ .
(b).....	0.6	-	-	15	
(b) Albumin.....	0.4	-	-	15	
(b) Globulin.....	107	-	-	15	From the fistular juice in 3 subjects.
Urea (mg/l).....	trace	-	-	16	
Creatinine.....	2	-	-	16	
Uric acid (mg/l).....	-	(85-180)	-	16	From the fistular juice in 1 subject
Reducing substances (as glucose) (mg/l).....	5.2	-	-	2	Cholesterol has not been found in the fistular juice ¹⁵ .
Lipids (mg/l).....	Pancreatic juice is rich in enzymes and their precursors. The principal enzymes are the zymogens of proteases and peptidases such as trypsinogen, chymotrypsinogen and procarboxypeptidases, small amounts of amylase, lipase, phospholipase, ribonuclease, deoxyribonuclease, clostridiopeptidase A and pancreatopeptidase E are also present ¹⁸ . The fistular juice contains proteolytic enzymes ²⁰ as well as amylase and lipase ^{14, 21} . The presence of a trypsin inhibitor in the pancreatic juice has also been reported ²² . The pancreatic juice is often free of enzymes, and their absence is not a specific feature of cystic fibrosis ^{4, 23} . The enzyme content is increased after injection of acetylcholine or pancreozymin and after vagus stimulation.
Enzymes					
By pancreozymin test ^{7, 8, 24, 25}	0.62	0.29-1.30	-	25	See remarks under 'Chymotrypsin', 'Trypsin' and 'Lipase' opposite.
Amylase (mg/min).....	0.72	0.36-1.45	-	25	
Carboxypeptidase A (mg/min).....					

Pancreatic Juice

(For references see page 653)

The pancreatic juice probably arises from two different types of cells: the one type, presumably the epithelial cells of the ducts, secrete a very watery juice rich in bicarbonate, whereas the other type, the epithelial cells of the acini, produce a viscous secretion rich in enzymes. Various stimuli, for instance acids, bring about the liberation of secretin and pancreozymin from the duodenal mucosa. Secretin stimulates mainly the secretion of fluid and bicar-

bonate, while pancreozymin, acetylcholine and vagus stimulation cause an increase in the liberation of enzymes. Unless stated, the data given in the table below apply to unstimulated pancreatic juice obtained either by means of intubation (here duodenal contents) or an external pancreatic fistula. For further information on the pancreatic juice see the literature¹⁻³.

	Mean	95% range (extreme range in brackets)	<i>s</i>	Reference	Remarks
Physicochemical data					
Appearance					Watery, colourless, thin fluid, clear or slightly opalescent. Because of its tendency to solubilise, the pancreatic juice is also known as abdominal salt.
Secretion rate (ml/h)					
Young children	—	(4-13)	—	4	"
Adults	36	(>0-99)	—	2	"
Secretin test ¹⁻³					
(ml/h)	176	38-314	69	2	"
(ml/h/kg body weight)	2.68	1.04-4.32	0.82	2	"
Specific gravity	—	(1.008-1.011)	—	11-13	
Freezing-point depression (°C)	—	(0.55-0.63)	—	12-13	The pancreatic juice is roughly isotonic with the serum.
Water (g/l)	987	—	—	11	
Dry substance (g/l)	13.0	(7.5-15.7)	—	14	Values from fistular juice in 2 subjects. About 50-60% of the dry substance is inorganic.
pH value	—	(7.5-8.8)	—	15-16	

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Inorganic substances					
Bicarbonate (mEq/l).....	-	(25-[150])	-	17	The bicarbonate content of pancreatic juice rises in the form of a hyp curve from 25 mEq/l at a secretory rate of 40 ml/h up to 130-150 mEq/l at a secretory rate of 300 ml/h. The sum of the bicarbonate and chloride con- tions is constant and amounts to about 154 mEq/kg water ¹⁷ .
Secretin test ⁶⁻⁹					
(mEq/h).....	13.5	0-27.1	6.8	9	Values from 47 adults with a healthy pancreas, obtained by analysi pancreatic juice during the hour following intravenous injection of 2 u secretin per kilogramme body weight. The results of the test in adu almost independent of sex and age ¹⁰ . The bicarbonate concentration creased in chronic pancreatitis.
(mEq/h/kg body weight) ...	0.199	0.047-0.351	0.076	9	
(mEq/l)	76	62-90	7	9	
Chloride (mEq/l).....	-	([4]-129)	-	17	The chloride content of pancreatic juice is determined by the bicarl content (see under 'Bicarbonate' above). With increasing secretory r chloride content falls in the form of a hyperbolic curve.
Phosphate (mmol/kg water)	0.8	0-1.6	0.4	17	From analysis of the duodenal contents. The values accord with the fistular juice ¹⁶ .
Potassium (mEq/l)					
(a).....	-	(6-9)	-	17	In (a) duodenal contents, (b) fistular juice.
(b).....	-	(4.1-5.5)	-	16	
Sodium (mEq/l)	-	(139-143)	-	17	From analysis of the duodenal contents; in agreement with values fro fistular juice of 3 subjects ¹⁵ . The sodium content of the pancreatic juice l parallels that of the serum.
Calcium (mEq/kg water)...	3.4	2.2-4.6	0.6	17	From analysis of the duodenal contents; in agreement with values fro fistular juice of 3 subjects ¹⁵ .
Magnesium (mEq/kg water)	1.0	-	-	17	From analysis of the duodenal contents.
Other minerals	The following have also been found in the fistular juice ¹ : sulphur (b sulphate ¹⁵), silicic acid, zinc (a component of carboxypeptidase A) and of copper.
Organic substances					
Total nitrogen (g/l)	-	(0.76-0.98)	-	1	Results of analyses of fistular juice made during the period 1902-1912.
Nonprotein nitrogen (g/l) .	0.14	-	-	15	From the fistular juice in 3 subjects.
Proteins (g/l)					
(a).....	-	(4.8-5.3)	-	18	Values from (a) duodenal contents of 3 subjects, (b) fistular juice of 3 sub
(b).....	-	(1.9-3.4)	-	15	The greater part of the proteins in pancreatic juice are enzymes and their cursors, the remainder plasma- and mucoproteins. Electrophoretic separ has yielded up to 7 fractions ¹⁴ .
(b) Albumin	0.6	-	-	15	
(b) Globulin	0.4	-	-	15	
Urea (mg/l).....	107	-	-	15	From the fistular juice in 3 subjects.
Creatinine	trace	-	-	16	
Uric acid (mg/l).....	2	-	-	15	
Reducing substances (as glucose) (mg/l)	-	(85-180)	-	16	From the fistular juice in 1 subject.
Lipids (mg/l)	5.2	-	-	2	Cholesterol has not been found in the fistular juice ¹⁵ .
Enzymes	Pancreatic juice is rich in enzymes and their precursors. The principi zymes are the zymogens of proteases and peptidases such as tryptic chymotrypsinogen and procarboxypeptidases; small amounts of amyl lipase, phospholipase, ribonuclease, deoxyribonuclease, clostridiopeptida and pancreatopeptidase E are also present ¹⁹ . The fistular juice contains teolytic enzymes ²⁰ as well as amylase and lipase ^{14,21} . The presence trypsin inhibitor in the pancreatic juice has also been reported ²² . The creatic juice is often free of enzymes, and their absence is not a specific fea of cystic fibrosis ^{4,23} . The enzyme content is increased after injectio acetylcholine or pancreozymin and after vagus stimulation.
Bypancreozymin test ^{7,8,24,25} :					
Amylase (mg/min)	0.62	0.29-1.30	-	25	} See remarks under 'Chymotrypsin', 'Trypsin' and 'Lipase' opposite.
Carboxypeptidase A (mg/min)	0.72	0.36-1.45	-	25	

(For references see page 656)

	Hepatic bile				Gallbladder bile				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
Dry substance (g/l).....	20	(8-34)	9	6	136	(70-248)	60	6	About 85-95% of the dry substance is organic. Water and salts are absorbed in the gallbladder, so that the increase of concentration of the gallbladder bile involve mainly the organic constituents; concentration is also aided by the release of mucopolysaccharides from the gallbladder epithelium.
	-	(23-33)	-	7	180	-	-	7	
	33.9	28.9-38.9	2.5	8	166	(144-219)	-	9	
pH value	7.15	-	-	10	6.89	-	-	10	Gallbladder bile is rather more acid than hepatic bile, possibly as a result of the enzymatic formation of lactic acid in the gallbladder.
	7.5	(6.2-8.5)	-	11	6.0	(5.6-8.0)	-	11	
Inorganic substances									
Bicarbonate (mEq/l).....	30	-	-	10	19	-	-	10	Like the bicarbonate content of the pancreatic juice, that of the bile increases as the rate of secretion increases ² .
Chloride (mEq/l).....	100.6	(89-118)	-	12	31	(7-110)	-	13	
Total phosphorus (g/l) ...	0.148	0.060-0.236	0.044	7	1.40	-	-	7	Most of the phosphorus is contained in phospholipids.
Potassium (mEq/l)	4.98	(2.6-12.0)	-	12	13.5	(8.4-17.5)	-	13	
Sodium (mEq/l)	148.9	(131-164)	-	12	220	(146-360)	-	13	The magnesium content of the bile is roughly the same as that of the serum ¹⁸ .
Calcium (mEq/l).....	-	(3.3-4.1)	-	14	15.4	(3.9-33.2)	-	13	
Magnesium	The bile contains small amounts of zinc and manganese.
Iron (mg/l)	-	(0.4-3.1)	-	1	-	(0.6-3.8)	-	1	
Copper (mg/l)	-	(0.35-2.05)	-	16					The bile contains small amounts of zinc and manganese.
Other minerals	
Organic substances									
Total nitrogen (g/l)	0.72	(0.24-1.45)	0.31	6	3.49	(1.88-6.00)	1.45	6	The total nitrogen of gallbladder bile fluctuates widely because of the variable bilirubin and protein content. About 40% of the nitrogen of gallbladder bile is dialysable ¹⁸ .
	0.77	(0.68-0.92)	-	7	4.9	-	-	7	
					2.8	(1.6-3.3)	-	17	
Nonprotein nitrogen (g/l)	0.46	-	-	19	-	(0.68-0.94)	-	19	Most of the nonprotein nitrogen is due to bilirubin, choline (component of the phospholipids), urea and amino acids (mainly glycine and taurine as components of the bile-acid conjugates).
					2.7	-	-	17	
Peptide nitrogen (mg/l)...	140	-	-	19	-	(39-270)	-	19	Choline is contained in the phospholipids.
Amino-acid nitrogen (mg/l).....	54	-	-	19	-	(60-216)	-	19	
Urea (mg/l).....	236	-	-	19	-	(200-450)	-	19	Free bilirubin does not occur in the bile: 70-80% of the bilirubin of gallbladder bile and over 90% of that of hepatic bile occur as bilirubin diglucuronide, the remainder as bilirubin monoglucuronide ²⁰ . Apart from bilirubin, bile contains also small amounts of other bile pigments ^{1,21} . The bilirubin content of gallbladder bile is decreased in cirrhosis of the liver ²² .
Choline (g/l)	0.57	0.22-0.92 (0.35-0.89)	0.175	7	5.5	-	-	7	
Bilirubin (g/l)	0.65	(0.12-1.35)	0.13	6	2.94	(0.36-6.30)	1.94	6	The porphyrins consist of coproporphyrin I and III ¹ .
	-	(0.26-0.41)	-	7					
Porphyrins (μg/l)	101	-	-	23	

	Hepatic bile				Gallbladder bile				Remarks
	Mean	95% range (extreme range in brackets)	s	Refer- ence	Mean	95% range (extreme range in brackets)	s	Refer- ence	
*Proteins (g/l)	1.8	(1.4-2.7)	-	7	4.5	-	-	7	The bile proteins consist of plasma proteins, mucopolysaccharides and enzymes. The presence of various plasma proteins has been demonstrated immunologically ^{17, 24} , namely albumin, orosomucoid, α -haptoglobin, transferrin and γ -G-globulin, as well as others specific to bile ²⁵ . The albumin fraction of hepatic bile is diminished in acute icterogenic hepatitis, while the other protein fractions are increased ²⁶ .
Enzymes	The bile contains many enzymes ^{10, 27, 28} , including salivase, phosphatase A, lipase, amylase, lactate dehydrogenase, malate dehydrogenase, transaminase, alkaline phosphatase, acid phosphatase, leucine aminopeptidase, L-isoleucine dehydrogenase, glucose 6-phosphate dehydrogenase, creatine kinase, and fructose diphosphate aldolase. The concentration of many of these enzymes in gallbladder bile is about 10 times their concentration in the serum ²⁷ .
Total carbohydrates (g/l)	-	(0.35-0.91)	-	7	2.4	-	-	7	The carbohydrates in hepatic bile mainly consist of glycoproteins ⁸ (see also under 'Proteins', above), those in gallbladder bile of mucopolysaccharides ^{10, 24} . These mucopolysaccharides form a complex with the lipids and bilirubin ^{10, 20} . Also found in gallbladder bile are galactose, glucose, small amounts of alobiose, fucose and ribose, glucosamine, galactosamine and uronic acids ⁸ . The carbohydrate content of gallbladder bile is markedly lower than in the presence of stones ¹⁰ .
Hexosamine, bound (mg/l)	57	(5-160)	49	6	83	(30-180)	53	6	The reducing substances probably consist mainly of glucose ⁸ .
Reducing substances (as glucose) (g/l)	-	(0.17-0.52)	-	7	0.8	-	-	7	
Lactic acid (mg/l)	-	-	-	-	-	(130-480)	-	30	
Lipids	-	-	-	-	-	-	-	-	In addition to bile acids the main lipids of bile are lecithin and cholesterol, also present are triglycerides, diglycerides and non esterified fatty acids ^{21, 22} .
Total fatty acids (g/l)	2.7	(1.6-4.1)	-	7	2.4	-	-	7	About 80% of the fatty acids consist of palmitic, oleic and linoleic acids ²² . Non-esterified fatty acids make up only about 0.5% of the total lipids ²² .
Phospholipids (g/l)	-	(1.0-4.3)	-	7	3.4	(15-53)	-	30	Lecithin accounts for about 98% of the phospholipids, the remainder consisting of cephalins and lysolipids ²¹ . In acute icterogenic hepatitis the phospholipid content of the bile is reduced ²⁶ .
Cholesterol (g/l)	-	(0.20-0.22)	-	28	-	(0.78-0.81)	-	25	
Children	-	(0.8-1.8)	-	7	6.3	(3.1-16.2)	-	26	In gallbladder bile about 4% of the total cholesterol is esterified, the remainder free ²² . In acute icterogenic hepatitis the cholesterol content of the bile is reduced ²⁶ .
Adults	-	-	-	-	-	-	-	-	
Bile acids (g/l)	-	(6.5-14)	-	7	115	-	-	7	
	-	-	-	-	32.1	0-65.9	16.9	28	For other values see page 656. The bile acids in bile are mostly conjugated with glycine and taurine, only a small proportion being in the free form ²⁷ . In bile the bile acids are present as the anions. They include small quantities of trihydroxycoprostanoic acid ²⁹ , which is secreted in the liver from cholesterol, the primary bile acids (choleic and chenodeoxycholic acids), which are likewise formed in the liver, and the secondary bile acids (deoxycholic, lithocholic and ursodeoxycholic acids), which are formed in the intestine by bacterial action from the primary bile acids, are there absorbed and again excreted in the bile ²⁸ . Since bacteria are absent from the newborn intestine the bile of newborn...

Bile acid content of the bile in children and adults

Age	Number of subjects	Bile acids (mEq/l)*		Ratio glycine:taurine		Ratio cholic acid : chenodeoxycholic acid : deoxycholic acid
		Mean	Range	Mean	Range	
Hepatic bile (A fraction) ⁴²						
1-4 days	13	10.7	4.6-26.7	0.47	0.21-0.86	2.5:1:-
5-7 days	17	11.3	2.0-29.2	0.95	0.34-2.30	2.5:1:-
7-12 months	8	8.8	2.2-19.7	2.4	1.4 -3.1	1.1:1:-
4-10 years.....	3	3.4	2.4- 5.2	1.7	1.3 -2.4	2.0:1:0.9
20 years.....	19	8.1	2.8-20.0	3.1	1.9 -5.0	1.2:1:0.6
Gallbladder bile ³⁷						
Over 20 years.....	4	121	31.5-222	3.0	1.0 -6.6	1.0:1:0.5

* 1 mEq corresponds to ca. 0.4 g free bile acids.

* 1 mEq corresponds to ca. 0.4 g free bile acids.

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Intestinal Juice

The composition of the secretions of the various parts of the healthy human gut is unknown since it is impossible to obtain pure samples. The composition of the intestinal contents, however, has been determined¹. The main constituents of the intestinal juice,

apart from electrolytes, are proteins² (albumin, γ -globulins, mucoproteins, enzymes) and lipids². The rate of flow of plasma into the jejunum is about 0.20 ml/10 cm/h, or 0.036 ml/cm²/24 h².

Electrolyte content of the intestinal secretion in dogs⁴

	Duodenum	Jejunum	Ileum	Colon		Duodenum	Jejunum	Ileum	Colon
Volume (ml/h)	6-38	4-88	11-42	1-10	Chloride (mEq/l) ..	103-139	141-155	68-88	60-88
pH	6.5-7.6	6.3-7.3	7.6	7.9-8.0	Potassium (mEq/l) ..	5-9	4-10	5	6-9
Carbon dioxide (mmol/l)	-	5-27	70-97	86-93	Sodium (mEq/l) ...	138-156	126-152	146-156	136-151
					Calcium (mEq/l) ..	-	2-3	5	4-5

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	Mean	95% range (extreme range in brackets)	n	Reference	Remarks
Physicochemical data					
Appearance	Meconium Soft, sticky, homogeneous mass, odourless and <i>greenish brown to black</i> in colour. Infants' stools <i>Golden yellow</i> (bilirubin) on breast milk, turning <i>green</i> (biliverdin)
Odour . . .					Typical odours are due to volatile degradation products of protein
Amount					
Meconium (g) . . .	-	(70-90)	-	5	Values from (a) 44 children, (b) 24 male adults. The amount excreted daily depends on the amount and nature of the diet. Infants on breast milk excrete less faeces (ca 15-25 g/24 h) than those on cow's milk (ca 30-40 g/24 h).
(a) Children's stools, 2 months-6 years (g/24 h)	-	(6.6-54.1)	-	6	For adults the daily amount after long fasting falls to 9.5-22 g, on a purely meat diet it is 54-64 g, on a purely vegetable diet ca 370 g, in disease daily amounts of 500-1200 g or more occur ^d
(b) Adult stools (g/24 h)	115.3	33.1-197.5	41.1	7	
Number of stools per day					
Children					
1 day	-	(3-4)	-	9	69% of 500 healthy newborn infants had their first stools within 12 hours, 94% within 24 hours ¹⁰
1 week	-	(4-5)	-	9	
2 weeks	-	(3-4)	-	9	
3-6 weeks	-	(2-3)	-	9	
7-13 weeks	-	(1-2)	-	9	
Water					
(a) Meconium (g/kg)	774	712-836	31	11	Values from (a) 12, (b) 44, (c) 7 subjects
(b) Children's stools, 2 months-6 years (g/kg)	-	(623-857)	-	6	
(c) Adult stools (g/kg)	750	-	-	12	
(g/24 h)	111	-	-	12	
Dry substance					
Meconium (g/kg)	276	-	-	13	
(a) Children's stools, 2 months-6 years (g/24 h)	-	(2.0-12.9)	-	6	
(b) Adult stools (g/24 h)	34.0	1.6-66.4	16.2	7	statist.
(c) Adult stools (g/24 h)	21	11-31	5	12	
Ash (% of dry substance)					
Meconium	4.0	-	-	13	
Adults	20	-	-	1	
Calorific value					
(kcal/g dry substance)	5.15	(4.21-5.99)	-	15	Value
(kcal/24 h)	139	< 213 (upper limit of normal)	-	15	utiliz.
pH value					
Meconium	6.1	(5.7-6.4)	-	16	The
Infants' stools, 6 days (on breast milk)	4.9	(4.6-5.2)	-	16	"
Adult stools	7.15	5.85-8.45	0.65	17	...

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Ions (mEq/kg) (anions or cations in solution)	-	(180-220)	-	20	Among the cations in solution are the sodium, potassium and ammonium an part of the calcium and magnesium, among the anions organic acids, free fat acids, bicarbonate, chloride and part of the phosphate ²¹⁻²³ .
Inorganic substances					
Bicarbonate (mEq/kg)	< 30	-	-	22	
Chloride (mEq/24 h)	-	(0.5-3.0)	-	24	With an average chloride intake of 50-150 mEq/24 h.
Phosphorus					
(a) Meconium (mmol/kg) . . .	5.28	2.38-8.18	1.45	11	Values from (a) 12 infants, (b) persons with an average phosphorus intake of 25-50 mmol/24 h. Most of the phosphorus is present as calcium phosphate, a small part as phosphate ion in solution ^{22,23} .
(b) Adult stools (mmol/24 h)	-	(10-25)	-	24	
Sulphate	0	-	-	22	
Fluoride (mg/24 h)	-	(0.5-2.2)	-	25	With an average fluorine intake of 1.5-4.7 mg/24 h.
Iodine (µg/24 h)	-	(10-57)	-	26	Values from 7 persons.
Potassium					
(a) Meconium (mEq/kg) . . .	31.4	11.8-51.0	9.8	11	Values from (a) 12 infants, (b) persons with an average potassium intake of 50-75 mEq/24 h, (c) 7 adults.
(b) Adult stools (mEq/24 h) .	-	(5-15)	-	24	
(c) Adult stools (mEq/24 h) .	11.3	3.3-19.3	4	12	
Sodium					
(a) Meconium (mEq/kg) . . .	136	90-182	23	11	Values from (a) 12 infants, (b) persons with an average sodium intake of 50-150 mEq/24 h, (c) 7 adults.
(b) Adult stools (mEq/24 h) .	-	(0.5-5.0)	-	24	
(c) Adult stools (mEq/24 h) .	6.5	0.5-12.5	3	12	
Calcium					
(a) Meconium (mEq/kg) . . .	23.2	6.5-39.9	8.35	11	Values from (a) 12 infants, (b) persons with an average calcium intake of 25-75 mEq/24 h. In adult stools about 10 mEq/24 h is of endogenous origin (intestinal secretions) ²⁷ .
(b) Adult stools (mEq/24 h) .	-	(15-65)	-	24	
Magnesium					
(a) Meconium (mEq/kg) . . .	39.2	18.2-60.2	10.5	11	Values from (a) 12 infants, (b) persons with an average magnesium intake of 20-40 mEq/24 h.
(b) Adult stools (mEq/24 h) .	-	(10-30)	-	24	
Iron					
(a) Meconium (mg/kg)	16.8	(12.0-27.1)	-	28	Values from (a) 6 infants, (b) persons with an average iron intake of 7 mg/24 h.
(b) Adult stools (mg/24 h) . .	-	(5.7-6.7)	-	29	
Copper					
Meconium (mg/kg)	17.0	(9.5-24.7)	-	28	Values from 6 infants.
Adult stools (mg/24 h)	1.96	0-4.62	1.33	30	
Zinc					
Meconium (mg/kg)	65.0	(38.8-117)	-	28	
Adult stools (mg/24 h)	-	(5.1-10.3)	-	31	
Cobalt (µg/24 h)	-	(0.19-1.21)	-	32	
Manganese (mg/24 h)	3.69	0-8.29	2.30	30	
Other elements	The amounts of aluminium, lead and tin are of the same order as those in the food ³⁰ . On strontium excretion see SCHMID and ZIPP ³³ , on strontium in meconium see WIDDOWSON ¹¹ .
Nitrogenous substances					
Nitrogen					
Meconium (g/kg)	19	-	-	13	Values from (a) 24, (b) 7 persons. The nitrogenous components are from mucus and epithelial cells of the intestinal wall and from digestive juices, bacteria and food. 17% of the nitrogen is in the bacterial fraction; about 47% of it is water-soluble ^{1,2} . During fasting about 0.25 g nitrogen per day is excreted in the stools ¹ . The nitrogen content is increased in some types of diarrhoea, as well as in pancreatic disease and steatorrhoea.
Infants' stools (g/24 h)					
On breast milk	0.16	-	-	1	
On cow's milk	0.4	-	-	1	
Adult stools (g/24 h)					
(a)	1.8	-	0.2	7	
(b)	1.1	-	-	12	

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Proteins	—	—	—	—	The proteins consist mainly of undigested nutrient proteins and bacterial proteins, with only a very small proportion of plasma proteins, most of which are specific substances.
Amino acids	—	—	—	—	In children's stools free amino acids represent only a small part of the total nitrogen. ³⁸
Ammonia (mg/kg)	—	(251-884)	—	27	Ammonia arises in the terminal intestine from bacterial action.
Porphyrins					
Coproporphyrin (mg/24 h)	0.422	0.012-0.832	0.205	32	Deutero- and mesoporphyrin are also present. ³⁹ The porphyrin contents of faeces increased in idiopathic steatorrhea ³⁸ and some porphyrias. ⁴⁰
Protoporphyrin (mg/24 h)	0.955	0-2.09	0.567	32	
Bilirubin					
Meconium (mg/kg)	585	(252-1020)	—	40	As determined, 'urobilinogen' includes various colourless and coloured bacterial breakdown products of bilirubin (particularly urobilinogen and urobilin). Urobilinogen is rarely found in the stools in the first week of life as it is present only in small and fluctuating quantity during the first year. ⁴¹ Cf. bilirubin breakdown see page 362.
Adult stools (mg/24 h)	—	(5-20)	—	41	
Urobilinogen (mg/24 h)					
Men	101	(57-200)	—	42	As determined, 'urobilinogen' includes various colourless and coloured bacterial breakdown products of bilirubin (particularly urobilinogen and urobilin). Urobilinogen is rarely found in the stools in the first week of life as it is present only in small and fluctuating quantity during the first year. ⁴¹ Cf. bilirubin breakdown see page 362.
Women	40	(80-150)	—	42	
Purine bases					
As nitrogen (mg/24 h)	—	(63-73)	—	44	Uric acid is also present in small amount in the stools and meconium. ⁴
Enzymes					The enzymes arise from digestive secretions, cells of the intestinal wall and bacteria.
Trypsin (mg/g)	0.065	—	—	45	Meconium contains no trypsin. ⁴⁶ In chronic pancreatitis the trypsin or chymotrypsin content of the stools is often lowered. ⁴⁸
Chymotrypsin (mg/g)	0.421	—	—	46	
Non-nitrogenous substances					
Carbohydrates (g/kg)					
Children, up to 1 year	—	(< 8)	—	47	In the faeces of healthy adults these consist solely of indigestible polysaccharides from food, such as cellulose and hemicellulose. Mono- and disaccharides are found occasionally in infants' stools, glucuronic acid in the stools of newborn.
Adults	0	—	—	47	
Organic acids (mEq/kg)	150	(100-400)	—	28	Organic acids make up rather more than 50% of the anions of faeces and arise from bacterial decomposition of carbohydrates. See also below under 'Volatil fatty acids' and 'Lactic acid'.
Lactic acid (mg/24 h)					
(a) Children	160	(4.5-370)	—	38	Values from (a) 11, (b) 28 subjects. Often increased when absorption of carbohydrate is disturbed.
(b) Adults	32.4	0-76.4	22	49	
Phenols (mg/24 h)	—	(20-80)	—	49	Breakdown products of aromatic amino acids.

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Total fats (g/24 h)					
(a) Children, 2 months-6 years	-	(0.29-1.79)	-	6	Values from (a) 44 children by the SPERRY method, (b) 14 and (c) 24 adults by the method of VAN DE KAMER et al. ⁵² . On a fat-free diet the daily fat excretion is about 2 g ⁵³ . In adult stools about 15% of the lipids are in the bacterial fraction ⁵² . The fat content is increased in various forms of malabsorption, i too rapid passage of food through the intestine, in biliary and pancreatic disease and in obstruction of the flow of lymph from the intestine. Steatorrhoe is better diagnosed by determining the fat content of the 24-hour stools than from the dry substance ⁴ ; the microscopic examination of undigested food residues is diagnostically useless ^{4,54} .
(b) Adults	5.54	0.14-10.94	2.7	51	
(c) Adults	4.0	0.8-7.2	1.6	7	
As percentage of dry substance					
(a) Children, 2-6 months ...	-	(5.2-43.1)	-	6	
(a) Children, 6 months-6 years	-	(6.1-25.8)	-	6	
(c) Adults	13.3	-	8.07	7	
Free fatty acids (g/24 h)					
(a) Children, 2 months-6 years	-	(0.14-1.38)	-	6	
(b) Adults	3.96	-	2.28	50	
Volatile fatty acids (mEq/24 h)					
	-	(9.8-31.2)	-	55	Acetic, propionic, butyric, valeric and other volatile fatty acids arise from bacterial decomposition of carbohydrates in the intestine; they are increased in sprue.
Neutral sterols					
Meconium (g/kg)	7.9	-	-	56	The ratio of sterol esters to free sterols is about 0.15. In adults the sterol consist of about 60% coprosterol, 15% cholesterol + cholestanol, 4% 7-de hydrocholesterol + Δ^7 -cholestenol, 17% plant sterols ⁵³ .
Children's stools (g/24 h)					
1st week	0.24	-	-	56	
7 weeks-10 months	0.10	-	-	56	
Adult stools (g/24 h)	-	(0.39-0.76)	-	57	
Bile acids (g/24 h)					
	-	(0.27-0.48)	-	57	Estimated range. The following bile acids have been identified in faeces ⁵⁸ : chenodeoxycholic acid, cholic acid, deoxycholic acid and lithocholic acid. The bile acid content varies with the nature of the nutrient fat ⁵⁹ .
Vitamins					
Vitamin B₆ (mg/24 h)					
Infants	-	(0.15-0.30)	-	60	
Adults	-	(0.7-0.9)	-	60	
Vitamin B₁₂ (µg/24 h)					
	~10	-	-	61	
Ascorbic acid (mg/24 h) ...					
	-	(<10)	-	62	

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The physical properties and chemical composition of urine are very variable and change considerably with the amount and nature of the diet, while the amounts of endogenous metabolites present depend also on the body weight. The composition of individual urine samples does not tally precisely with that of the 24-hour urine since the excretion of many constituents is subject to a day-night rhythm¹⁻³. Unless otherwise stated, the data given in this chapter are for adults on a mixed diet. There is an extensive literature on the properties and composition of urine⁴⁻⁶.

Appearance

At the moment of voiding, the urine is usually clear and transparent, though a highly alkalizing meal may sometimes cause it to be more or less cloudy. When clear urine has stood for a while a opulent turbidity (nubecula) appears, this is due to the presence of mucus from the urinary tract and, in alkaline urine, of various crystals (metallic phosphates). Turbidity of the urine may also be due to lipids.

The cell content of urine is discussed on page 677, urinary sediments on pages 677–678.

Colour

Urine normally has a more or less intense yellow colour, but the


severe sweating

Yellowish red to brick red In the presence of urobilinogens or porphobilinogens

sulphonphthalein

Blue In the presence of indigo carmine.

Odour

	Mean	95% range (extreme range in brackets)		Refer- ence	Remarks										
Amount (ml/24 h)															
Newborn, infants															
1 day	17	(0–68)	—	9	Values from (a) 60, (b) 40 and (c) 27 subjects (the last group over 90 years of age). At birth the bladder contains up to 44 ml (mean 5.7 ml) of urine ¹² . Premature infants secrete less urine than full-term infants of the same age ¹³ . The excretion of urine is correlated with high plasma glucose ¹⁴ .										
2 days	34	(0–84)	—	9											
3–10 days	—	100–300	—	9											
10 days–2 months	—	250–450	—	9											
2–12 months	—	400–500	—	9											
Children															
1–3 years	—	500–600	—	9											
3–5 years	—	600–700	—	9											
5–8 years	—	650–1000	—	9											
8–14 years	—	800–1400	—	9											
(a) Men	1015	(510–2000)	—	10											
(b) Women	989	(500–1875)	—	10											
(c) Aged persons	853	(273–2400)	—	11											
(ml/kg body weight/24 h)															
(a) Newborn, 1st day	8.5	1.5–15.5	3.5	12	Values from (a) 9 infants, (b) 15 infants (breast-fed) and (c) 11 men										
(b) Newborn, 7th day	76	42–110	17	12											
(c) Young men	20	13.6–26.4	3.2	12											
Specific gravity															
Newborn, first days	1.012	—	—	9	The specific gravity of individual samples of urine can vary between 1.001 and 1.050 ¹⁵ . For calculation of the amounts of solutes from the specific gravity see under "Dry substance" on page 662. The maximum specific gravity in the fluid deprivation test is discussed under "Renal Function Values" on page 530. The specific gravity of urine is greatly reduced in diabetes insipidus but increased in diabetes mellitus, fever and the nephrotic syndrome (as a result of proteinuria).										
Infants	—	(1.002–1.006)	—	9											
Adults	—	(1.010–1.025)	—	12											
Relative viscosity															
	—	(1.0–1.14)	—	12											
					<table><tr><th>Specific gravity</th><th>Relative viscosity</th></tr><tr><td>1.005</td><td>1.0</td></tr><tr><td>1.015</td><td>1.02</td></tr><tr><td>1.022</td><td>1.09</td></tr><tr><td>1.024</td><td>1.14</td></tr></table> <p>(Viscosity of distilled water = 1.00)</p>	Specific gravity	Relative viscosity	1.005	1.0	1.015	1.02	1.022	1.09	1.024	1.14
Specific gravity	Relative viscosity														
1.005	1.0														
1.015	1.02														
1.022	1.09														
1.024	1.14														
					The viscosity is increased when the urine contains increased amounts of albumin, blood or erythrocytes.										
Surface tension (dyn/cm⁻¹)															
	—	(64–69)	—	4											

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks	
Freezing-point depression (°C)						
(a)	—	(0.1–2.5)	—	19	Values (a) are for the limiting dilution and concentration capacities of neurons, values (b) for adults with maximum urinary concentration. For n of determination see JOHNSON et al. ²¹ . The osmolarity and osmolality are almost equal. Newborn infants, and particularly premature infants, c concentrate the urine only up to 700–1100 mosm/l depending on the urea c tration ²² .	
(b)	—	(1.6–2.5)	—	20		
Osmolarity (mosm/l)						
(a)	—	(50–1400)	—	19		
(b)	—	(855–1335)	—	20		
pH value						
Newborn	6.2	—	—	23	Normal urine usually has an acid reaction due to the phosphoric and sul acids arising from breakdown of proteins. On a vegetable diet it may b alkaline as a result of breakdown of organic acids from fruit and vegeta bicarbonate. The pH value (and the titratable acidity) is subject to a da night rhythm ^{1, 26} . The urine is least acid (sometimes alkaline) on wak the morning and most acid towards midnight. It may also become al owing to bacterial decomposition of urea.	
Infants	6.0	(5.1–6.8)	—	23, 24		
Children	—	(5.3–7.2)	—	24		
Men	5.7	(4.8–7.5)	—	19, 25		
Women	5.8					
Titratable acidity (mEq/kg body weight/24 h)						
(a) Newborn	0.30	—	—	23	Titration up to pH 7.4; values from (a) 20, (b) 220 and (c) 11 subject titratable acidity depends on the amounts of acids (uric, lactic and keto and primary phosphates present. In the newborn the urine has only a titratable content ^{16, 28} . In adults the total acidity (titratable acidity + NH a mixed diet averages 50–60 mEq/24 h ²⁹ (see also pages 535–536). In s nonrenal acidosis up to 1000 mEq hydrogen ions may be excreted daily, w alkalosis bicarbonate excretion may result in a daily saving of up to 250 hydrogen ions. In stationary renal acidosis an average of 19 mEq hydro ions is retained daily ³⁰ .	
(b) Infants	0.96	—	—	23		
(c) Young men	0.64	0.39–0.89	0.125	16		
Men (mEq/24 h)	38	(20–40)	—	25, 27		
Women (mEq/24 h)	28					
Dry substance (g/24 h)	—	(50–72)	—	2	The amount of solutes in the urine can be calculated roughly from the sp gravity by multiplying the second and third decimal places by 2.6 (1 small children). Example: specific gravity 1.020; dry weight $\approx 20 \times 2$ 52 g/24 h (adults) ⁶ .	

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Inorganic substances (for references see pages 664–665)

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Chloride (mEq/kg body weight/24 h)					
(a) Newborn, 1st day	0.43	0.07–0.79	0.18	1	Values from (a) 9 infants, (b) 16 infants (breast-fed) and (c) 11 men. Ab 80–95% of the ingested chloride is excreted in the urine. The chloride excreti is increased on a high-salt diet, by the action of diuretic agents, in renal tubu injury (salt-losing nephritis) and in Addison's disease; it is decreased on lo salt diets, in chloride loss due to vomiting, sweating or diarrhoea, in Cushing syndrome and corticosteroid treatment, and in all forms of salt retention su as oedema.
(b) Newborn, 7th day	2.08	0.08–4.08	1.00	1	
(c) Young men	2.80	1.56–4.04	0.62	1	
Men (mEq/24 h)	184	(120–240)	—	2, 3	
Women (mEq/24 h)	132				

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Phosphorus (mg/kg body weight/24 h)					
(a) Newborn, 1st day	0.12	0.06-0.18	0.03	¹	Values from (a) 9 infants, (b) 16 infants (breast fed, about 10 times higher on cow's milk) and (c) 11 men. The urine secreted in utero contains only little phosphorus ¹ . About 95-100% of the urinary phosphorus is in the inorganic
(b) Newborn, 7th day	0.32	0-0.7	0.19	¹	
(c) Young men	16.5	10.1-22.9	3.2	¹	
Adults (g/24 h)	-	(0.8-2.0)	-	⁴	phate resorption, or the phosphate excretion index ⁸ , for values measured in children see JANSE et al. ¹⁰ . For further data on phosphorus excretion see NIOSOM ¹¹ and BOREL ¹¹
Sulphur (g/24 h)					
Total S	1.32	(1.24-1.49)	-	¹²	phate resorption, or the phosphate excretion index ⁸ , for values measured in children see JANSE et al. ¹⁰ . For further data on phosphorus excretion see NIOSOM ¹¹ and BOREL ¹¹
Inorganic sulphate-S	1.17	(1.07-1.30)	-	¹²	
Sulphuric ester-S	0.09	(0.08-0.10)	-	¹²	
Neutral S	0.07	(0.05-0.08)	-	¹²	
Inorganic sulphate-S (mg/kg body weight/24 h)					
(a) Newborn, 1st day	3.4	0-6.8	1.7	²	Values from 8 subjects
(b) Newborn, 7th day	6.0	1.8-10.2	2.1	¹	
(c) Young men	19.2	10.8-27.6	4.2	¹	
SO ₄ ²⁻ (mEq/24 h)					
Men	45	(30-70)	-	^{2,3}	Values from (a) 31 infants, (b) 28 infants, (c) 34 adults with a drinking-water fluoride content of 0.5-0.6 mg/l, (d) 5 adults with a fluoride intake of 1.3-4.7 mg/24 h. Fluoride excretion falls at the 4th month of pregnancy (to 0.22 mg/l at the 8th month) and rises after parturition to normal in 16 weeks ¹²
Women	36				
Bromide (mg/l)	6.56	(2.97-8.55)	-	¹⁸	
Fluoride (mg/l)					
(a) Children, 1-3 years	0.14	(0.05-0.30)	-	¹⁶	Values from (a) 31 infants, (b) 28 infants, (c) 34 adults with a drinking-water fluoride content of 0.5-0.6 mg/l, (d) 5 adults with a fluoride intake of 1.3-4.7 mg/24 h. Fluoride excretion falls at the 4th month of pregnancy (to 0.22 mg/l at the 8th month) and rises after parturition to normal in 16 weeks ¹²
(b) Children, 4-6 years	0.27	(0.05-0.70)	-	¹⁸	
(c) Adults	0.52	(0.30-0.85)	-	¹⁸	
(d) Adults (mg/24 h)	-	(0.9-2.9)	-	¹⁷	
Iodide (mg/24 h)	0.191	(0.018-0.483)	0.138	¹⁹	
Thiocyanate (mg/l)	4	(0-6)	-	²⁰	In nonsmokers, higher in smokers.
Cyanide (μg/24 h)	-	(2-6)	-	²¹	
Carbon dioxide (mmol/24 h)	-	(0.3-3.0)	-	³	In physical solution in urine at pH 5.5-6.0, with rising pH carbon dioxide is increasingly present as bicarbonate. See also under 'pH value' and 'Titratable acidity' above
Potassium (mEq/kg body weight/24 h)					
(a) Newborn, 1st day	0.36	0.08-0.64	0.14	¹	In physical solution in urine at pH 5.5-6.0, with rising pH carbon dioxide is increasingly present as bicarbonate. See also under 'pH value' and 'Titratable acidity' above
(b) Newborn, 7th day	0.95	0-2.25	0.65	¹	
(c) Young men	1.05	0.79-1.31	0.13	¹	
Men (mEq/24 h)	57	(35-80)	-	^{2,3}	
Women (mEq/24 h)	47				
Sodium (mEq/kg body weight/24 h)					
(a) Newborn, 1st day	0.25	0.11-0.39	0.07	¹	
(b) Newborn, 7th day	1.73	0-4.36	1.29	¹	
(c) Young men	2.66	1.58-3.74	0.54	¹	
Men (mEq/24 h)	177	(120-220)	-	^{2,3}	
Women (mEq/24 h)	123				

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Calcium (mEq/kg body weight/24 h)					
(a) Newborn, 1st day	0.02	0.01-0.03	0.005	24	Values from (a) 12 infants, (b) 9 infants (breast-fed; about one-half as much on cow's milk), (c) 104 children, (d) 121 adults and (e) 13 adults. 0-33%, mean 22%, of the urinary calcium is ionized, the remainder bound to organic acids ²⁹ . Calcium excretion is subject to a day-and-night rhythm with a maximum during the morning and a minimum during the night ^{7,8} , probably an effect of meals ³⁰ . It is more dependent on the degree of absorption from food than on the calcium content of the diet; with an intake of 700 mg calcium per day about 30% is excreted in the urine. In adults the calcium excretion is <i>decreased</i> when the calcium content of the diet is low and also in persons of advanced age ³¹ . Unlike the serum calcium level, calcium excretion does not change significantly during pregnancy ³² . It is pathologically <i>increased</i> in hyperparathyroidism, various forms of osteoporosis, bone metastases, tubular acidosis, idiopathic hypercalcaemia and vitamin-D poisoning, <i>decreased</i> when the calcium serum level is low (as in hypoparathyroidism and osteomalacia with steatorrhoea) and in renal insufficiency (for instance in the nephrotic syndrome). On calcium excretion see the literature ^{11,33} .
(b) Newborn, 7th day	0.26	0.18-0.34	0.04	25	
(c) Children, 1 year	0.10	(0.01-0.40)	-	26	
(d) Adults	-	(0.05-0.31)	-	27	
(e) Adults (mEq/24 h)	11.5	6.5-16.5	2.5	28	
Magnesium (mEq/kg body weight/24 h)					
(a) Newborn, 1st day	0.004	0.0004-0.0076	0.0018	24	Values from (a) 12 infants, (b) 13 infants (breast-fed; about one-half as much on cow's milk), (c) 91 men, (d) 61 women. The magnesium excretion is subject to a day-and-night rhythm with a maximum during the morning and a minimum during the night ^{8,37} , probably an effect of meals ³⁰ . Of the magnesium in the diet about one-third is absorbed and excreted in the urine. An increase in magnesium excretion has been recorded during medication with diuretic agents ³⁸ .
(b) Newborn, 7th day	0.050	0-0.118	0.034	34	
(c) Men (mEq/24 h)	10.7	4.7-16.7	3.0	35	
(d) Women (mEq/24 h)	8.8	3.4-14.2	2.7	36	
(e) Adults (mEq/24 h)	-	(4.9-16.5)	-	36	
Iron (µg/24 h)					
(a)	55	-	-	39	Values (b) from 10 subjects determined with bathophenanthroline. The iron arises mainly from erythrocytes and from epithelial cells of the renal tubules and vesical mucosa. Iron excretion is increased in diseases involving intravascular haemolysis ⁴¹ .
(b)	100	(40-150)	-	40	
Copper (µg/24 h)					
(a) Children	12	(6-17)	-	42	Values from (a) 12 children, (b) 20 adults, (c) 12 adults and (d) 16 subjects; values (a) and (b) determined with oxalyldihydrazide, (c) with dithizone, (d) by neutron activation analysis. Copper excretion is at a maximum in the afternoon. It is pathologically <i>increased</i> in Wilson's disease, portal vein cirrhosis and proteinuria (for instance in the nephrotic syndrome), with 60-80% of the copper present as caeruloplasmin.
(b) Adults	14	(8-22)	-	42	
(c) Adults	18	3.6-32.4	7.2	43	
(d)	50.4	28.2-72.6	11.1	44	
Manganese (µg/24 h)	0.8	0.2-1.4	0.3	44	Values from 16 subjects determined by neutron activation analysis. See also KEHOE et al. ⁴⁵ and SCHROEDER ⁴⁶ .
Molybdenum (µg/l)	16.3	0-42.7	13.2	47	Values from 16 subjects determined by emission spectrography. See also SCHROEDER ⁴⁶ and MELTZER et al. ⁴⁸ .
Zinc (µg/24 h)					
(a)	457	217-697	120	49	Values from (a) 14, (b) 16 subjects. Zinc excretion is increased in liver cirrhosis due to alcohol ⁴⁹ , in diabetes ⁴⁸ and in cancer ⁴⁷ .
(b)	430	138-722	146	47	
Other elements	Urine also contains silicate ⁵ , nitrite and nitrate ⁵ , and borate ⁵⁰ . The arsenic content is normally less than 0.1 mg/l ⁵¹ , the lead content 30-80 µg/l ^{46,52} ; the mercury content should not exceed 30 µg/l ⁵³ . The following elements have also been determined in urine: aluminium ⁴⁵ , cadmium ^{46,48,50} , chromium ^{46,50} , cobalt ⁴⁸ , nickel ^{45,46,50,54} , silver ⁴⁶ , strontium ^{24,25,55} , titanium ⁴⁶ , vanadium ⁴⁶ , bismuth ⁴⁸ and tin ^{45,46,48} .

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nitrogenous substances (for references see pages 671-672)

	Mean	95% range (extreme range in brackets)	#	Reference	Remarks
Total nitrogen (g/l)					
(a) Newborn, at birth . .	0.74	0.02-1.46	0.36	1	V-1
(b) Newborn, 2nd day . .	6.40	3.44-9.36	1.48	1	
(c) Adults . .	9.19	-	-	2	
(mg/kg body weight/24 h)					
(a) Newborn, 1st day	38.9	2.1-75.7	18.4	1	4, nit
(b) Newborn, 2nd day	75.4	23.6-127	25.9	1	
(d) Newborn, 7th day	108	65.8-150	21.1	1	
(e) Young men	207	159-255	24.2	1	
(g/24 h)					
(f) Children, 3-11 years	-	(5.3-20.9)	-	3	
(g) Adults . .	11.5	6.9-16.1	2.3	4	
Urea (mg/kg body weight/ 24 h)					
(a) Newborn, 0-2 days	39	-	-	2	V-1
(b) Newborn, 4-6 days	73	-	-	2	
(c) Adults	358	-	-	2	
(d) Adults (g/24 h)	20.6	12.6-28.6	4.0	4	
Creatine (mg/kg body weight/24 h)					
(a) Premature infants, 2-12 weeks	2.3	(0.3-4.3)	-	6	
(b) Newborn, 2-12 weeks	28.0	(15.2-35.8)	-	7	
(c) Infants, 6-12 months	10.6	(3.6-15.3)	-	7	
(d) Children, 6-11 years	4.0	(2.2-7.4)	-	8	
(mg/24 h)					
(e)	-	(0-50)	-	9	
(f)	-	(18.6-58.5)	-	10	
(g) Men	52.1	(11-189)	-	11	
(g) Women	92.1	(19-270)	-	11	
(h) Persons over 90 years	90	(25-230)	-	12	
Creatinine (mg/kg body weight/24 h)					
(a) Premature infants, 2-12 weeks	14.3	(8.3-19.9)	-	6	
(b) Newborn, 2-12 weeks	11.9	(11.0-14.6)	-	7	
(c) Infants, 6-12 months	9.8	(5.2-20.4)	-	7	
(d) Children, 6-11 years	16.3	(6.4-21.9)	-	8	
(g/24 h)					
(e) Men, 20-45 years	1.80	1.1-2.5	0.95	16	
(f) Women, 20-45 years	1.17	1.01-1.33	0.08	16	
(g) Persons over 90 years	0.47	(0.04-1.0)	-	12	

	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Remarks
Guanidine (mg/24 h).....	-	(<2)	-	16	
Guanidinoacetic acid					
(a) Newborn, 2-12 weeks (mg/kg body weight/24 h)	2.6	(1.7-3.6)	-	17	Values (a) by chromatographic separation in 11 infants, (b) colorimetrically in 5 adults.
(b) Adults (mg/24 h).....	27	(11-56)	-	18	
Methylguanidine (mg/24 h)	-	(<1)	-	16	
Ammonia (mg/24 h)					
Men	680	(340-1200)	-	19	Values from (a) 9 infants, (b) 16 infants (breast-fed) and (c) 11 men. Abnormally low values are found in alkaline urine as a result of loss of ammonia, abnormally high values in old urine samples as a result of bacterial formation of ammonia. The ammonia excretion is proportional to the anionic content of the diet (for instance phosphates and sulphur in meat); it is therefore higher in acid than in alkaline urine. It is pathologically <i>increased</i> in metabolic and respiratory acidosis, <i>decreased</i> in metabolic and respiratory alkalosis and in injury to the distal renal tubules.
Women	510				
(mEq/24 h)					
Men	40	(20-70)	-	19	
Women	30				
(mEq/kg body weight/24 h)					
(a) Newborn, 1st day.....	0.26	0.02-0.50	0.12	1	
(b) Newborn, 7th day	0.56	0.26-0.86	0.15	1	
(c) Young men	0.80	0.52-1.08	0.14	1	
Amino acids, total					
(mg/24 h).....	2255	(1337-3150)	-	20	Calculated from the amounts of the individual amino acids in hydrolysed urine.
(mg α -amino-N/24 h).....	261	-	-	20	
Amino acids, free (mg/24 h)					
(a)	800	(350-1180)	-	21	Values (a) calculated from the amounts of the individual free amino acids (see the table on page 667); values (b), (d), (e) determined colorimetrically with ninhydrin; values (c) determined as the copper complex; values (d) from 8, (e) from 18 subjects. For details see page 667.
(mg α -amino-N/24 h)					
(b) Children, 2-4 years.....	33	(16-54)	-	22	
(a) Adults	90	(41-133)	-	21	
(mg α -amino-N/kg body weight/24 h)					
(c) Premature infants, 2-12 weeks	20.7	(10.0-26.8)	-	6	
(c) Newborn, 2-12 weeks ...	12.9	(6.8-20.7)	-	7	
(c) Infants, 6-12 months ...	6.3	(3.4-8.5)	-	7	
(c) Children	1.8	(0.9-2.9)	-	23	
(a) Adults	1.4	(0.6-2.1)	-	21	
(mg α -amino-N/mg creati- nine-N)					
(d) Children.....	0.46	0.14-0.78	0.16	24	
(e) Adults	0.17	0.08-0.26	0.045	24	
Amino acids, bound (excluding peptides)					
<i>o</i> -Aminobippuric acid (mg/24 h).....	1.14	(0.4-1.7)	-	28	Values from 20 subjects. See also under ' <i>o</i> -Aminobenzoic acid', page 669.
Hippuric acid (g/24 h)	-	(1.0-2.5)	-	29	
<i>m</i> -Hydroxyhippuric acid (mg/24 h).....	6	(2-150)	-	30	Represents about 70% of the bound glycine. The benzoic acid from which the hippuric acid arises mostly originates from aromatic components of vegetable foods. Hippuric acid excretion is <i>increased</i> after ingestion of large amounts of fruit and vegetables, pathologically <i>decreased</i> in renal insufficiency.
Phenylacetylglutamine (g/24 h)	-	(0.25-0.50)	-	29	
Peptides (mg/24 h)					
Anserine	-	(5-7)	-	31	For a summary of data see SKARŻYŃSKI and SARNECKA-KELLER ³³ .
Carnosine.....	-	(2-3)	-	31	
Homocarnosine	1.1	(0.5-2.4)	-	32	
Peptides containing hydroxy- proline (as hydroxyproline)	25.1	(14.0-38.7)	-	34	Values from 12 adults. The excretion is increased in growing children ³⁵ . Only traces of free hydroxyproline are present in urine. The hydroxyproline excretion is a measure of the collagen metabolism.

Amino acid	mg/24 h						μmol/kg body weight/24 h***					
	Children* (9-24 months)		Men**		Women**		Premature infants, bottle-fed	Full-term babies and infants		Children	Adults	
	Mean	Extreme range	Mean	Extreme range	Mean	Extreme range		Bottle-fed	Breast fed			
Alanine	10	5-15	22	5-32	24	9-44	18.6-125	14.2-30.2	9.6-15.3	3.2-18.2	3.6-9.8	
β-Alanine	ca. 0.3	-	6	3-10	3	2-9	-	-	-	-	-	
α-Aminoadipic acid	ca. 0.5	-	8	5-13	4	0-13	-	-	-	-	-	
α-Aminobutyric acid	ca. 0.3	-	-	-	-	-	-	-	-	-	-	
γ-Aminobutyric acid	ca. 0.3	-	-	trace	-	trace	-	-	-	-	-	
β-Aminoisobutyric acid	5	0-9	22	6-37	29	10-52	-	<2.7	3.2-12.2	1.4-9.4	-	
Arginine	ca. 0.5	-	6	0-14	4	0-11	<3.1	<1.3-7.1	<1.0	-	<0.7-2.0	
Asparagine	-	-	-	-	-	-	-	-	-	-	3.9-7.8	
Aspartic acid	-	<4	8	3-29	4	2-11	-	-	-	-	<1.2	
Citrulline	-	-	-	-	-	-	-	3.9-6.2	4.4	-	-	
Cystine	-	-	-	-	-	-	<3.1-8.1	1.1-7.7	<2.9	0.6-4.1	<0.5-1.2	
Cystine + cysteine†	-	<4	14	3-33	6	0-13	-	-	-	-	-	
Glutamic acid	-	-	-	-	-	-	2.3-31	2.3-13.1	5.2	1.5-1.6	<0.7-2.8	
Glutamine	-	-	-	-	-	-	-	-	-	4.0-33.4	-	
Glutamine + asparagine	25	2-60	73	42-103	62	43-88	-	-	-	-	-	
Glutamine + asparagine +serine	-	-	-	-	-	-	21.0-264	8.9-60.0	13.8-14.5	-	-	
Glycine	28	11-42	104	53-189	142	67-312	42.6-484	46.0-117	27.6-33.8	4.3-53.1	13.8-36.6	
Histidine	47	15-83	138	20-213	128	79-208	13.7-34.5	9.3-56.0	18.9-22.8	8.0-46.0	11.9-22.5	
Homocitrulline**	10	1-65	-	trace	-	trace	-	-	-	-	-	
Hydroxyproline***	-	0.8-1.4	-	<0.5	-	<0.5	-	-	-	-	-	
Isoleucine	-	<4	15	8-24	10	5-20	2.5-16.8	1.3-2.3	<1.5	0.5-2.3	1.1-2.7	
Leucine	-	<4	11	6-20	9	2-16	3.2-21	2.5-6.6	<3.7	0.7-3.1	1.0-2.3	
Lysine	10	1.5-20	7	0-14	8	0-16	-	-	-	1.8-23.5	0.7-4.5	
Lysine + 1-methylhistidine	-	-	-	-	-	-	10.6-35	7.0-27.0	9.7-10.1	-	-	
Methionine	-	<5	7	5-11	5	3-12	<2.6	0.5-1.3	<1.0	0.6-3.9	<0.6-1.2	
1-Methylhistidine	9	0-43	73	22-114	65	26-155	-	-	-	0.8-9.8	-	
3-Methylhistidine	-	<5	65	35-87	48	30-69	5.1-5.2	2.2-4.7	2.1-5.2	1.5-8.9	-	
Ornithine	-	<4	1	0-4	2	0-11	-	-	-	-	-	
Phenylalanine	-	<5	13	8-15	13	6-41	2.4-28	1.3-4.5	2.0-3.1	0.8-4.4	0.8-2.6	
Proline	ca. 0.3	-	-	-	-	-	0-108	0-37.6	0	0	<1.4	
Serine	7	7-13	42	27-65	37	22-61	-	-	-	4.1-22.4	3.9-7.8	
Taurine	10	2-14	123	44-231	87	27-161	<31	<16.5	3.5-7.3	2.2-45.3	9.1-38.6	
Threonine	6	3-9	17	2-35	23	5-33	11.3-140	4.0-20.0	3.8-5.6	2.4-10.3	1.9-5.0	
Tryptophan‡	-	-	21	10-32	16	5-27	-	-	-	-	-	
Tyrosine	-	<5	19	7-27	15	9-26	12.6-61	2.0-14.0	1.1-2.9	1.3-7.0	1.3-4.3	
Valine	ca. 0.3	-	10	4-17	6	0-30	1.9-23	<3.7	<1.9	0.5-2.0	<1.4	

* Values from 8 boys and 7 girls, determined by ion exchange chromatography (Bergman et al. *J Clin Invest* 50, 1973).

† Cystine 10-15 mg/l, cysteine 2-4 mg/l, determined by ion exchange chromatography (Bergman et al. *J Clin Invest* 50, 1973).

‡ Determined microbiologically (Ulrich, J A, *Proc Mayo Clin*, 29, 210 (1954)).

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Proteins (mg/24 h)					
Total non-dialysable material					
(a) Newborn	87.9	34.3–142	26.8	36	Values from (a) 7, (b) 3, (c) 11, (d) 7 subjects; values (a, b, c) by fractionation into protein and uromucoid by millipore filter; values (d) calculated from N-content of the non-dialysable material; values (e) by the biuret reaction; values (f) include about 80% chondroitin sulphate A. The discrepancy in values for high-molecular substances (between 30 and 750 mg/24 h ⁴⁷) are due in large part to the difficulty of concentrating the urine. These substances include 30–40% of carbohydrates ^{37, 42} , i.e., glycoproteins, glycopeptides and mucopolysaccharides. In electrophoretic separation of the proteins about 25% appear in the albumin fraction, 17% in the α_1 -globulin fraction, 24% in the α_2 -globulin fraction, 16% in the β -globulin fraction and 12% in the γ -globulin fraction ⁴³ . Up to 25 serum proteins have been identified in urine ⁴⁴ , including transferrin, γ A-globulin and γ G-globulin and also low-molecular γ -globulin chains; the other proteins present arise from the kidneys ⁴⁵ . The urinary protein content is physiologically increased in the newborn ⁴⁶ (particularly in premature infants), after standing erect with hyperlordosis following physical effort; it is pathologically increased in fever, severe shock and renal diseases (particularly the nephrotic syndrome ⁴⁷). In multiple myeloma a low-molecular protein (BENCE-JONES protein; for identification see SNAPP and ORES ⁴⁸ and NAUMANN ⁴⁹) often appears in readily identifiable amounts (precipitation with sulphosalicylic acid, disappearance of the precipitate 90–100 °C). For a detailed discussion of the proteins and mucopolysaccharides of urine see the literature ^{41, 49} .
(b) Infants	125	–	–	36	
(c) Adults	474	420–528	27	36	
(d)	433	203–663	115	37	
Proteins					
(a) Newborn	10.5	8.82–12.2	0.84	36	
(b) Infants	13.0	–	–	36	
(c) Adults	61.6	47.0–76.2	7.3	36	
(d)	204	–	–	37	
(e)	–	(30–60)	–	38	
Uromucoids					
(a) Newborn	4.75	3.27–6.23	0.74	36	
(b) Infants	14.8	–	–	36	
(c) Adults	70.5	47.7–93.3	11.4	36	
Mucopolysaccharides					
(f)	–	(3–15)	–	39	
Amines, betaines					
Ethanolamine (mg/24 h)					
(a) Children, 3–11 years	13.1	(3.6–18.7)	–	3	Determined (a) by column chromatography on 12 children, (b) by paper chromatography on 14 adults. Phosphoethanolamine occurs in the urine when the blood phosphatase level is low ⁵⁰ .
(b) Adults	20.6	(11.5–35.2)	–	18	
Methylamine (mg/24 h)	5.0	(4.6–6.0)	–	51	
Dimethylamine (mg/24 h)	17.0	(15.2–19.3)	–	51	
Cystamine (mg/24 h)	1.4	–	–	52	
Piperidine (mg/24 h)	5.7	(4.7–7.1)	–	51	Probably in the main of bacterial origin (large intestine) ⁵³ .
Choline (mg/24 h)	–	(5.6–9.0)	–	54	Present exclusively in the free form.
Carnitine (mg/24 h)	–	(80–130)	–	55	
Acetonitrile (μ g/l)	2.9	–	–	56	Values from nonsmokers; in smokers 118 μ g/l.
Tyramine (mg/24 h)	1.3	(0.8–2.6)	–	57	Probably in the main of bacterial origin (large intestine) ⁵³ .
Para-aminobenzoic acid (mg/24 h)	0.76	(0.31–1.32)	–	58	
Catecholamines (μg/24 h)					
Adrenaline free	1	–	–	59	Calculated from measurements on 41 samples of nocturnal urine. The catecholamines in urine are partly free, partly bound to sulphuric or glucuronic acid. See also page 733.
Noradrenaline free	57	–	–	59	
Dopamine free	197	–	–	59	
Metanephrine free	30	–	–	59	
total	88	–	–	59	
Normetanephrine free	205	–	–	59	
total	420	–	–	59	
Tryptophan metabolites	In vitamin B ₆ deficiency (see also pages 475–476) there is increased excretion of xanthurenic acid and other tryptophan metabolites, particularly after oral administration of tryptophan (tryptophan loading test) ^{60, 61} .
3-Hydroxyanthranilic acid (mg/24 h)	0.36	(0.1–1.1)	–	61	

Urine - Nitrogenous Substances

(For references see pages 671-672)

	Mean	95% range (extreme range in brackets)	n	Reference	Remarks
Hydroxykynurenine (mg/24 h).....	0.49	(0-2.3)	-	67	In women the excretion of this substance falls after menstruation
Acetylkynurenine (mg/24 h)	2.2	-	-	68	Values from 7 women
Kynurenine (mg/24 h)					
(a) Infants	2.32	(0.19-27.7)	-	69	Values from (a) 17, (b) 19, (c) 20 subjects
(b) Children.....	1.8	(0.50-3.8)	-	69	
(c) Adults	1.14	(0.3-2.6)	-	67	
Kynurenic acid (mg/24 h)					
(a) Infants	1.81	(0-4.75)	-	69	Values from (a) 17, (b) 19, (c) 20 subjects
(b) Children.....	5.0	(0.00-8.8)	-	69	
(c) Adults	2.83	(1.0-4.2)	-	67	
Xanthurenic acid (mg/24 h)					
(a) Children	6.4	(3.2-13.0)	-	69	Values from (a) 19, (b) 20 subjects. Found in only one of 6 gro
(b) Adults ..	0.66	(0.3-1.8)	-	67	(1.5 mg/24 h) ⁶³ .
<i>p</i> -Aminobenzoic acid (p-hydroxybenzoic acid) (mg/24 h)	0.89	(0.32-2.24)	-	69	Mainly present as <i>p</i> -aminohippuric acid (see page 666)
Nicotinic acid					See under 'Vitamins', page 477
<i>Indoles</i>					
Tryptamine (μg/24 h)					
(a) Children	-	(66-370)	-	69	Values from (a) 20, (b) 13, (c) 6 subjects. Probably in the ma
(b) Men	64	(20-120)	-	69	origin (large intestine) ⁶³
(c) Women	56	(40-72)	-	69	
<i>N,N</i> -Dimethyltryptamine (μg/24 h)	43.0	25.8-60.2	8.6	67	Values from 50 subjects
Serotonin (5-hydroxytryptamine) (μg/24 h)					
Free					
(a) Children	83	(43-123)	-	69	Values from (a) 6, (b) 20, (c) 6, (d) 21 subjects. The excretion
(b) Men	72	(45-110)	-	69	serotonin in particular is increased in sarcomatous tumours
(c) Women	55	(10-85)	-	69	
(d)	131	(31-296)	-	69	
As glucuronide	93	(21-355)	-	69	
As sulphate	59	(0-127)	-	69	
5-Hydroxyindoleacetic acid (mg/24 h)					
(a) Children	8.6	(1.4-13.2)	-	69	
(b) Adults	-	(1.0-14.7)	-	69	
(c) Adults	4.5	2.3-6.7	1.1	70	
5-Methoxytryptamine	0	-	-	69	50 μg/24 h has been found in the urine of a rheumatic fever;
Bufotenine (μg/24 h)	63	49-77	7	70	Values from 50 subjects
Indoxylsulphuric acid (mg/24 h)					
(a) Children	420	(143-620)	-	69	
(b) Adults	200	(140-250)	-	69	
(c) Men	64	28-100	18	70	
(d) Women	57	13-101	22	70	
6-Sulphatouracatole (mg/24 h)	24	(5-130)	-	69	

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Indole-3-acetic acid (mg/24 h)					
(a) Total	-	(5.2-13.8)	-	77	Values from (a, b) 11 subjects; (a) after hydrolysis of the urine.
(b) Free	-	(3.1-8.1)	-	77	
Indole-3-lactic acid (mg/24 h)	-	(0.3-3)	-	78	
Indolacetylglutamine (mg/24 h)	-	(1-8)	-	78	
Indoleformylglucuronide (mg/24 h)	-	(0-60)	-	79	
<i>Imidazoles, histidine metabolites</i>					
N-Acetylhistamine (µg/24 h)					
(a) Children	-	(17-1840)	-	85	Values from (a) 20, (b) 17 subjects. Probably in the main of bacterial o (large intestine) ⁵³ .
(b) Adults	22.0	(2.3-56)	-	80	
Histamine (µg/24 h)	11.9	(6.1-19)	-	80	The excretion of histamine and its metabolite 1,4-methylimidazoleacetic is considerably increased in mastocytosis ^{81,82} .
	-	(5-30)	-	81	
Imidazolelactic acid (mg/g creatinine)	19.8	9.6-30.0	5.1	83	Values from 12 subjects.
Urocanic acid (mg/24 h) ...	0.62	(0-1.7)	-	84	
Formiminoglutamic acid (formamidinoglutamic acid) (mg/24 h)	1.25	(0-2.1)	-	84	The excretion of this histidine metabolite is increased in folic acid deficiency (see page 479), sometimes also in vitamin B ₁₂ deficiency, diseases of the and sarcoidosis.
<i>Porphyryns and related compounds</i>					
Aminoacetone (mg/l)	2.2	(1.5-3.1)	-	85	
δ-Aminolaevulinic acid					
(a) Children (mg/l)	2.57	0.27-4.87	1.15	86	Values from (a) 50 children under 15 years, (b) 100 adults, (c) 13 adults. Or excretion in children of various ages see KASER et al. ⁸⁹ . It is increased in some porphyrias ⁹⁰ (see also pages 454-455) and in lead poisoning. Determination of this component in urine enables an increased absorption of lead to be recognized in time; concentrations of 13-20 mg/l urine correspond to 150-200 of lead per litre of urine and indicate that lead poisoning is imminent.
(b) Adults (mg/l)	2.9	0.1-5.7	1.4	87	
(c) Adults (mg/24 h)	2.63	0-5.33 (1.43-6.97)	1.35	88	
Porphobilinogen					
(a) Children (mg/l)	1.05	0.13-1.97	0.46	86	Values from (a) 50 children under 15 years, (b) 100 adults, (c) 13 adults. the excretion in children of various ages see KASER et al. ⁸⁹ . It is increased in some porphyrias ⁹⁰ (see also pages 454-455) and there is a slight increase in liver disease; it is not increased in lead poisoning.
(b) Adults (mg/l)	1.0	0-2.0	0.5	87	
(c) Adults (mg/24 h)	1.40	0.38-2.42	0.51	88	
Coproporphyrin					
(a) (µg/l)	70	0-150	40	87	Values from (a) 100, (b) 9, (c) 72 subjects. Spectrophotometric methods lower values than fluorometric methods (b) ⁹² . The excretion of coproporphyrin is proportional to the body weight ⁹¹ . 50-90% of the urinary coproporphyrin consists of coproporphyrin III, 10-40% of coproporphyrin I. The excretion is increased in some porphyrias ⁹⁰ (see also pages 454-455), liver disease and lead poisoning.
(b) (µg/24 h)	130	(80-220)	-	91	
(c) (µg/24 h)	36	6-66	15	92	
Uroporphyrin					
(a) (µg/l)	-	(0-15)	-	86	Values from (a) 25, (b) 9, (c) 72 subjects. Spectrophotometric methods lower values than fluorometric methods (b) ⁹² . The excretion of uroporphyrin is increased in some porphyrias ⁹⁰ (see also pages 454-455).
(b) (µg/24 h)	39	(28-63)	-	91	
(c) (µg/24 h)	12	4-20	4	92	
Bilirubin (mg/l)					
Children	0.9	-	-	95	
Adults	-	(0.02-1.9)	-	96	
Urobilinogen (mg/24 h) ...	0.36	0.05-2.5	-	97	Values from 46 subjects; the distribution is lognormal. Urobilinogen excretion is decreased in obstruction of the bile passages, increased in liver injury and in vascular haemolysis ^{97,98} .

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Enzymes (for definition of the unit U see page 584)

The healthy kidney excretes low-molecular enzymes and their products, such as amylase and uropepsinogen; if high-molecular enzymes are excreted at all they include lactate dehydrogenase¹⁻³, aspartate aminotransferase^{2,4}, ribonuclease⁵, alkaline phosphatase^{3,6,7}, acid phosphatase⁸, arylsulphatases⁹, β -glucuronidase¹⁰.

In renal injury the amounts of the enzymes in the urine are often increased. When determining enzyme activity in urine the urinary volume and diuretic state must be taken into account; thus the activity of some enzymes measured per unit volume of urine is higher in antidiuresis than in diuresis¹¹.

	Mean	95% range (extreme range in brackets)	s	Reference	Remarks
Amylase (kU/24 h, 37 °C) . . .	6.03	(2.06-11.8)	-	12	Frequently increased in acute pancreatitis.
Uropepsinogen (U/24 h, 37 °C)					
(a) Men	40	2-78	19	13	Values from (a) 21, (b) 18 subjects; substrate haemoglobin. A small amount of the pepsinogen secreted in the gastric mucosa enters the blood and is excreted by the kidneys; there is, however, little correlation between the uropepsin excretion and the pepsinogen content of the gastric juice. Absence of pepsinogen in the urine indicates atrophy of the gastric mucosa.
(b) Women	23	0-51	14	13	

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vary carbohydrates are present partly in the free form, components of glycoproteins, mucopolysaccharides and

glycopeptides, partly as glucuronic acid bound to phenols and acids. On free sugars in urine see SIMPSON¹.

	Mean	95% range (extreme range in brackets)	<i>n</i>	Reference	Remarks
substances (mg/24 h)	515	(242-845)	-	2	Values from 30 subjects by the NELSON-SOMMER method. The classical methods of determining 'sugar' are based on the reducing power of certain carbohydrates. The Nelson-Sommer method is based on the reduction of a copper salt by the hydrogenase reaction ⁵ .
(mg/l)					
born, 1st week	-	(<250)	-	6	Values (a) by means of chromatography, (b) from 20 subjects on a mixed diet.
born, 2nd week	-	(<200)	-	6	
s (mg/24 h)	72	(16-132)	-	2	Values (a) by means of chromatography, (b) from 20 subjects on a mixed diet.
e (mg/l)					tumours
born, 1st week	-	(<250)	-	6	Values (a) by paper chromatography, (b) from 10 adults on an average diet.
born, 2nd week	-	(<200)	-	6	Infants on a milk diet may excrete up to 400 mg galactose per litre urine, those with galactosaemia up to 10 g per litre ⁶ .
is	14	(3-25)	-	7	
t (mg/l)					
born, 1st week	-	(<700)	-	6	Values by paper chromatography. Fructose excretion is increased with a high fructose intake, idiopathic fructosuria is also known.
n, 2nd week	-	(<50)	-	6	
(mg/l)					
born, 1st week	-	(<1200)	-	6	Values (a) by paper chromatography, (b) from subjects on a mixed diet. No lactose is secreted when the diet is lactose-free. Endogenous lactose appears in the urine in late pregnancy and during lactation (up to 500 mg/l) ¹⁴ .
born, 2nd week	-	(<100)	-	6	
lis (mg/24 h)	25	(0-91)	-	6	
is					Sucrose may appear in the urine after oral masks ¹⁵ .
(mg/24 h)	49	(14-111)	-	7	Values from 10 adults on a mixed diet. The excretion of xylose and stabinose is increased after consuming fruit ¹⁶ .
ose (mg/24 h)	38	(12-56)	-	7	
ntoses (mg/24 h)	4.3	(0.5-8.1)	1.9	12	Values from 15 men. The ketopentoses consist mainly of L-xylose with traces of ribulose and sedoheptulose. In essential pentosuria 1-5 g L-xylose per day is excreted independently of the diet ¹⁷ .
l (mg/l)	-	(35-85)	-	14	Chromatographic studies showed meconititol in all samples and scyllitol in 67%.
onic acid, total 24 h)					
n	431	271-591	80	18	
men	371	193-549	89	18	
t body weight/24 h)					
wborn, 0-2 weeks	16.4	12.2-20.6	2.12	18	
wborn, 2-7 weeks	8.5	5.54-11.5	1.48	18	
lalyisable carbo- rates (mg/24 h)					
is	72.6	34.4-111	19.1	21	
amines	26.5	14.3-38.7	6.1	21	
icid	40.7	25.7-55.7	7.5	21	
onic acid, children	-	(4.1-14.7)	-	22	
onic acid, adults	-	(2.7-7.3)	-	22	

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	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
Organic acids (mEq/24 h)					
Men	55	-	-	1	Urine contains a large number of aliphatic and aromatic acids; in infant former dominate, in adults - depending on the intake of fruit and vegetables the latter. The aromatic acids are mainly bound to amino acids (page 666 details see the literature ^{2,3}).
Women	64	-	-	1	
Volatile acids (mg/24 h) ...	-	(8-50)	-	4	In the main formic acid, a little acetic acid and traces of butyric acid ² .
Formic acid (mg/l)	13	-	-	5	
Adipic acid (mg/24 h)	-	(1.3-2.5)	-	6	
Malic acid (mg/24 h)	5.4	-	-	7	
Succinic acid (mg/24 h)	-	(2-12)	-	8	
Pyruvic acid (mg/24 h)					
(a) Children	5.6	1.9-9.3	1.83	9	Values from (a) 21 children aged 5-10 years, (b) 3 men, (c) 3 women and children aged 3 months to 4 years. <i>Increased</i> in non-compensated diabetes
(b) Men	9.6	-	-	10	
(c) Women	11.4	-	-	10	
(mg/kg body weight/24 h)					
(d) Children	-	(0.16-0.52)	-	11	
Citric acid					
(a) Adults (mg/24 h)	462	90-834	186	12	Values from (a) 12 adults, (b) children aged 3 months to 4 years. Higher carbohydrate diet than on one rich in proteins, <i>increased</i> in treatment oestrogens (whence its fluctuation during the menstrual cycle) and vitamin <i>decreased</i> in severe muscular activity, acidosis, diabetes, hypoparathyroidism and chronic renal insufficiency ⁷ .
(b) Children (mg/kg body weight/24 h)	-	(4-12)	-	11	
Furane-2,5-dicarboxylic acid (mg/24 h)	-	(3-4)	-	13	
Glutaric acid (mg/24 h)	2.5	-	-	15	
α-Ketoglutaric acid (mg/24 h)					
(a) Children	9.3	0.5-18.1	4.4	9	Values from (a) 21 children aged 5-10 years, (b) 3 men, (c) 3 women and children aged 3 months to 4 years. <i>Decreased</i> in chronic renal insufficiency ⁷
(b) Men	12.0	-	-	10	
(c) Women	18.7	-	-	10	
(d) Children (mg/kg body weight/24 h)	-	(0.5-2.0)	-	11	
Methylmalonic acid (mg/24 h)	5.8	(0-11.2)	-	14	<i>Increased</i> in vitamin B ₁₂ deficiency.
Lactic acid (mg/24 h)	-	100-600	-	4	Often absent from the urine. <i>Increased</i> during severe muscular activity, ² following epileptic attacks and in fever.
Glycolic acid (mg/24 h)	42	-	-	16	Values from 15 children, adjusted to a body surface area of 1.73 m ² .
Glyoxylic acid (mg/24 h) ...	-	(1.4-4.7)	-	17	
Oxalic acid (mg/24 h)					
(a) Children	-	(10-45)	-	18	Values from (a) 25, (b) 18, (c) 60 subjects. In primary hyperoxaluria 100-400 g per day is excreted ²⁷ .
(b)	31	13-49	9	19	
(c)	-	(9.0-28.5)	-	20	
Ketone bodies (as acetone) (mg/24 h)					
(a)	-	(10-100)	-	22	Values (a) usual in adults; values (b) in young men. The ketone bodies consist of acetoacetic acid, β -hydroxybutyric acid (which must be oxidized before determination as ketone) and acetone; the proportion of β -hydroxybutyric acid increases as the total ketone-body excretion rises. <i>Increased</i> during fasting especially when physical work is done at the same time and when the ambient temperature is low; <i>decreased</i> in dehydration. It is <i>pathologically increased</i> in diabetes (up to 50 g/l in poorly adjusted patients), thyrotoxicosis and fever. Children are more inclined to hyperketonuria than adults.
(b)	209	(< 400)	-	23	
(c)	0.8	(0.2-2.5)	-	24	
Acetone (mg/l)					

	Mean	95% range (extreme range in brackets)	s	Refer- ence	Remarks
<i>mol</i> , aromatic acids	--	--	The aromatic acids are partly bound to amino acids (page 666), the phenols to glucuronic acid (page 673)
enol (mg/24 h)	10	(8-13)	-	26	
Cresol (mg/24 h).....	87	(64-117)	-	26	
catechol (mg/24 h)	5.7	-	-	26	
Methoxy-4-hydroxyphen- ylglycol (mg/24 h)	3.0	(1.4-4.6)	0.8	27	Values from 18 subjects
Methoxy-4-hydroxyphen- ylacetic acid (homovanillic acid) (mg/24 h) . .	5.35	3.2-7.6	1.1	28	Values from 15 young adults
vanillic acid (mg/24 h) . .	-	(<5)	-	29	
Methoxy-4-hydroxy- mandelic acid (mg/24 h) .	3.6	-	-	30	For further data see page 733
3-Hydroxyphenylacetic acid (mg/24 h) .	0.7	-	-	31	
3-Hydroxymandelic acid (mg/24 h)	0.4	-	-	30	
Homogentisic acid					Excreted in urine in measurable amount only in alkaptonuria (3-5 g/24 h) ³²
m-Hydroxybenzoic acid (mg/24 h)	-	(10-16)	-	32	
p-Hydroxyphenylacetic acid (mg/24 h)	-	(15-31)	-	32	
<i>Lipids</i>					
Non-dialysable lipids (mg/24 h)	15.6	0-31.8	8.1	34	Lipid content of the non-dialysable material in urine (see page 668), consisting of cholesterol, phospholipids and fatty acids, triglycerides are not normally present. Lipid excretion is increased in some kidney diseases, particularly the nephrotic syndrome
Cholesterol (mg/24 h)	2.7	(0.2-5.6)	-	35	Values from 5 subjects
Phospholipids (mg/24 h)	9.5	(7.0-13.3)	-	35	Values from 5 subjects

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- ²⁸ " "
- ²⁹ " "
- ³⁰ " "
- ³¹ " "
- ³² " "
- ³³ " "
- ³⁴ " "
- ³⁵ " "

	Mean	95% range (extreme range in brackets)		Refer- ence	Remarks
Coenzyme Q₁₀ (µg/24 h) ...	15.4	(0-58)	-	¹	
Thiamine (µg/l)					
(a)	900	(800-2400)	-	²	Values (a) from 31 subjects, using <i>Ochromonas danica</i> ² ; values (b) from 2 subjects, using <i>Ochromonas malhamensis</i> ³ ; values (c) on 24 infants during the three days. Except in dietary thiamine deficiency, the urinary thiamine excretion increases linearly with the intake. In thiamine deficiency it falls rapidly; whereas the excretion of thiamine metabolites remains largely constant (page 470). In beri-beri 0-14 µg thiamine are excreted daily ⁵ . Thiamine excretion is increased in diuretic treatment with mercury salts but not thiazides ⁶ .
(b)	-	(110-370)	-	³	
(c) Newborn	96	52-140	22	⁴	
Riboflavin					
(a) Newborn (µg/l)	219	157-281	31	⁴	Values from (a) 24 infants during the first three days, (b) 31 children, in of whom values were below 300 µg. Riboflavin excretion varies with dietary intake (see pages 471-472).
(b) Children, 3-7 years (µg/24 h)	-	(50-650)	-	⁷	
(c) Adults (µg/24 h)	-	(150-2000)	-	⁸	
Vitamin B₆ (µg/24 h)	40	(20-120)	-	⁸	Determined by means of <i>Tetrahymena pyriformis</i> .
(nmol/kg/h)					
Total	-	(0.55-1.24)	-	⁹	Values from 3 children and 3 adults. The free vitamin was determined by hydrolysis, the total vitamin after hydrolysis, in both cases using <i>Saccharo carlsbergensis</i> .
Free	-	(0.08-0.29)	-	⁹	
Pyridoxic acid	-	(1.7-8.0)	-	⁹	
Nicotinic acid					
(a) Children (mg/24 h)	2.3	(1.8-2.9)	-	¹⁰	Values determined (a) chemically, (b) microbiologically with <i>Tetrahymena formis</i> .
(b) Adults (mg/l)	-	(1.16-1.54)	-	³	
1-Methylnicotinamide (mg/24 h)					
(a) Newborn, 4-50 days	1.71	(0.55-4.87)	-	¹¹	Values from (a) 14, (b) 29, (c) 25 subjects. The excretion of this nicotinic metabolite is decreased in pellagra (see page 477).
(b) Children, 6-11 years	2.70	(0.77-5.45)	-	¹²	
(c) Men, under 35 years	7.38	(2.85-12.3)	-	¹³	
(c) Women, under 35 years ..	6.05	(2.34-12.7)	-	¹³	
(c) Men, over 50 years	3.60	(1.76-10.5)	-	¹³	
(c) Women, over 50 years ...	3.45	(1.50-9.20)	-	¹³	
1-Methyl-2-pyridone 5-carboxylamide (mg/24 h)					
(a) Newborn, 4-50 days	1.64	(0.30-6.67)	-	¹¹	Values from (a) 14, (b) 29, (c) 25 subjects. The isomeric compound 1-methyl-4-pyridone 5-carboxylamide is also present in urine ¹⁴ . The excretion of 1-methyl-2-pyridone 5-carboxylamide is increased during pregnancy ¹⁵ fluctuates during the menstrual cycle ^{15,16} ; it is pathologically decreased in diabetes ¹⁷ and pellagra (see page 477).
(b) Children, 6-11 years	4.47	(1.55-11.8)	-	¹²	
(c) Men, under 35 years	13.29	(4.44-29.2)	-	¹³	
(c) Women, under 35 years ..	11.14	(4.30-32.2)	-	¹³	
(c) Men, over 50 years	6.20	(0.80-21.1)	-	¹³	
(c) Women, over 50 years ...	12.28	(1.75-29.2)	-	¹³	
Vitamin B₁₂ (ng/24 h)	-	(0-27)	-	¹⁹	On a normal diet.
Folic acid (µg/24 h)	4	(2-7)	-	¹⁸	On a normal diet.
Biotin (µg/l)	-	(6.26-32.7)	-	³	Values determined with <i>Ochromonas danica</i> . Present in the urine in the free form.
Pantothenic acid (mg/l) ...	2.90	(0.76-4.1)	-	³	Values determined with <i>Lactobacillus plantarum</i> . Present in the urine in the free form.
Ascorbic acid					
(a) Newborn (mg/l)	45.4	31.8-59.0	6.8	⁴	Values (a) from 24 infants during the first three days. The values (b) for adults are dependent on the degree of tissue saturation and on the dietary intake (pages 489-490).
(b) Adults (mg/24 h)	-	(10-100)	-	-	

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	Mean	95% range (extreme range in brackets)	<i>n</i>	Refer- ence	Remarks
erythrocytes (per ml)	—	0-2500	—	¹	On the erythrocyte contents of the urine of newborn infants see Aas ² , on that of pregnancy urine see SCHOLTZ ³ . The erythrocyte content may be increased in spastic contraction of the renal veins (as for instance in haematuria due to lordotic congestion) as also in various diseases of the kidneys and urinary tract, including kidney stone and bladder stone.
r 24 h	130000	—	—	2	
leucocytes (per ml)	—	0-3000	—	¹	On the leucocyte content of the urine of newborn infants see Aas ² , on that of pregnancy urine see SCHOLTZ ³ . The leucocyte content is increased in all inflammatory renal diseases.
en (per h)	46000	(0-220000)	—	1	
omen (per h)	74000	(0-574000)	—	1	
r 24 h	650000	—	—	2	
yaline casts (per 24 h)	2000	—	—	2	73% of all sediments contain no hyaline casts.
acteria	—	—	—	—	—

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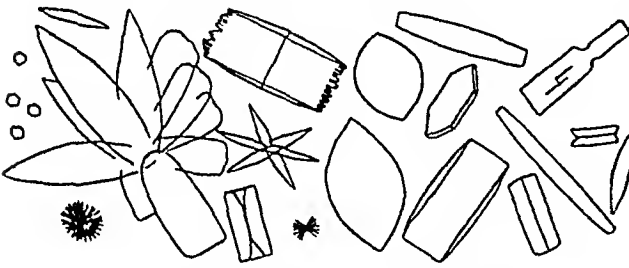
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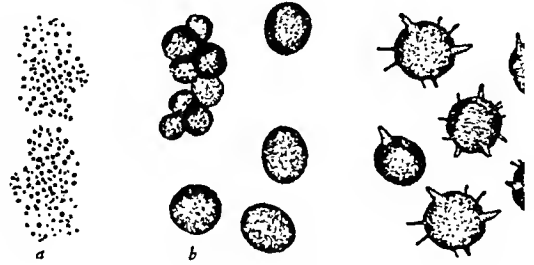
Amorphous and crystalline chemical sediments

Sediment	Characteristics	Occurrence	Solubility (○ = readily soluble, ● = sparingly soluble)						
			Heating	Alkalies	Mineral acids	Acetic acid	Alcohol	Acetone	Ether
Uric acid	Crystals mostly, but not always, coloured yellow by absorption of urinary pigments	Acid urine	○ (60°C)	○	●	●	●	●	●
Urites	Calcium, magnesium and potassium urates, mostly amorphous, in concentrated acid urine. Colour and chemical behaviour as for uric acid	Ammonium urate in alkaline urine. All other urates in acid urine	○ (60°C)	○	●	●	●	●	●
Phosphates									
Calcium phosphate	Rare	Alkaline urine	●	●	○	○	●	●	●
Ammonium magnesium phosphate	Commonest	Alkaline urine	●	●	○	○	●	●	●
Calcium oxalate	Same about that of erythrocytes	Usually in acid urine, also in neutral and weakly alkaline	●	●	○	●	●	●	●
Cystine	Colourless crystals (distinguish from uric acid crystals, when of similar form). Must be looked for in fresh urine since cystine is rapidly destroyed by bacteria	Acid urine	●	○ (rel- ative)	○	●	●	●	●
Tyrosine	Often yellow-coloured since they are associated with leucine. Usually accompanied by leucine. Occur in acute yellow atrophy of the liver, also in chronic acute phosphorus poisoning, leukaemia	Acid urine	● (rel- ative)	○	○	○	●	●	●
Leucine	See tyrosine. Crystals in urine are impure. Pure leucine crystallizes in hexagonal plates	Acid urine	○ (rel- ative)	○	○	○	●	●	●
Bilirubin (haematoidin)	Colours any uric acid crystals present and changes their shape	Acid urine	●	○	○	○	●	○	●
			readily soluble in chloroform						
Indigotin	Rare. Also colours other crystals and thus appears in crystalline in various forms. Pure indigo in urine is amorphous or as <i>β</i> as in the figure on page 678. Crystallizes from chloroform as <i>ε</i> in this figure	Alkaline or acid urine	very soluble in chloroform			●	—	○	○
Cholesterol	Very rare	Acid urine	very soluble in chloroform			●	—	○	○
Hippuric acid	Very rare		○	○	○	●	—	○	○
Sulphonamides	Easily distinguished from uric acid crystals by solubility in acetone		—	—	—	—	○	—	—

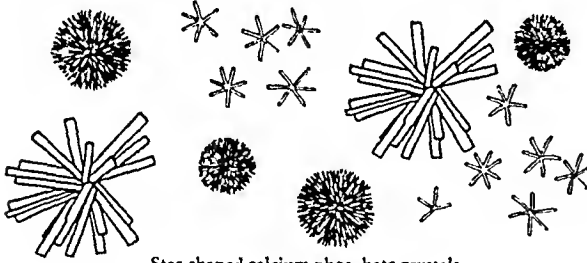
Amorphous and crystalline chemical sediments¹



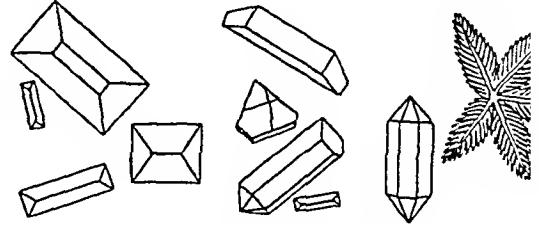
Various crystalline forms of uric acid



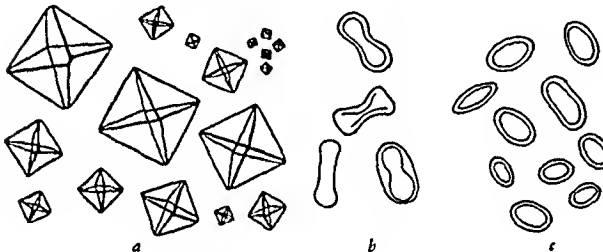
Urates



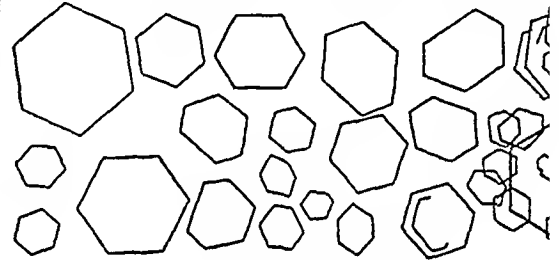
Star-shaped calcium phosphate crystals



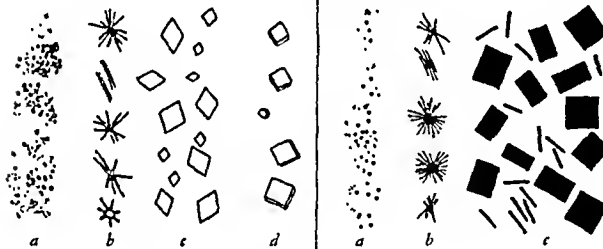
Ammonium magnesium phosphate crystals



Calcium oxalate crystals

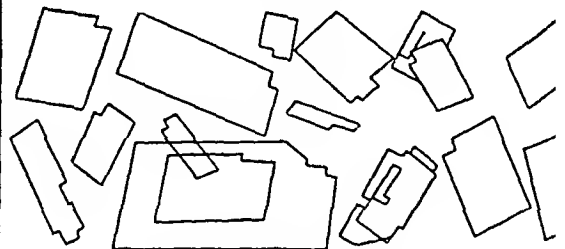


Hexagonal cystine crystals

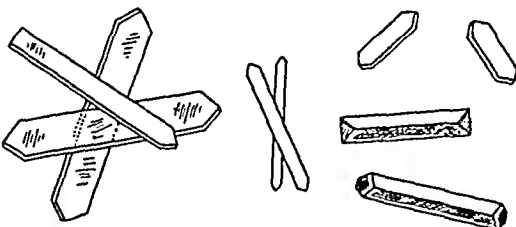


Bilirubin

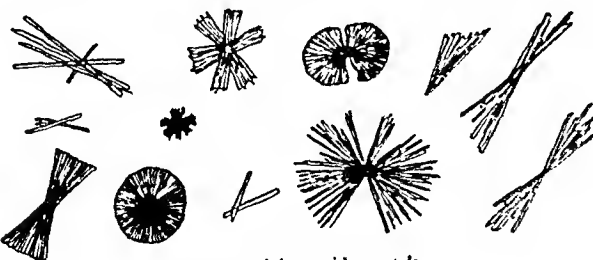
Indigotin



Jagged cholesterol platelets



Hippuric acid



Various sulphonamide crystals

- | | |
|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Urates | <p><i>a</i> calcium, magnesium and potassium urates mostly amorphous</p> <p><i>b</i> ammonium urate (spherical forms)</p> <p><i>c</i> sodium urate (thorn-apple forms)</p> |
| Calcium oxalate | <p><i>a</i> octahedra, often flattened (commonest)</p> <p><i>b</i> dumb-bell forms</p> <p><i>c</i> ring forms</p> |
| Bilirubin
<i>reddish brown</i> | <p><i>a</i> amorphous</p> <p><i>b</i> masses of needles</p> <p><i>c</i> rhombic forms</p> <p><i>d</i> cubic forms</p> |
| Indigotin
<i>blue</i> | <p><i>a</i> amorphous</p> <p><i>b</i> masses of needles</p> <p><i>c</i> rectangular platelets from chloroform</p> |

¹ From HARRISON, G.A., *Chemical Methods in Clinical Medicine*, 4th ed., Churchill, London, 1957, pages 100 et seq.

Sweat

(For references see page 681)

Sweat is secreted by two kinds of gland, the small, eccrine sweat

gland, the rate of secretion and the location. There is an extensive literature on the composition of eccrine sweat¹⁻⁶.

Approximate numbers of sweat glands*

Total....	2 million
Forearm of elbow	751/cm ²
Palm of hand	373/cm ²
Chest	155-250/cm ²
Buttocks	57/cm ²

gland, so that unless otherwise stated the data in the

Eccrine sweat unless otherwise stated	Mean	95% range (extreme range in brackets)	n	Reference	Remarks
Physicochemical data					
Appearance	Eccrine sweat: clear, watery, odourless. Apocrine sweat: cloudy, viscous, often slightly yellow and fluorescent, sometimes bluish or blackish (chromhidrosis or excessive coloration), sterile apocrine sweat is odourless but rapidly acquires its characteristic smell from bacterial action (bromhidrosis or osmidrosis = development of excessive odour)
Amount (l/24 h)					
(a)	0.3-0.5	-	-	7	(a) Insensible perspiration = macroscopically invisible sweat and transepidermal water loss
(b)	(2-3)	-	-	7	
Specific gravity	-	(1.001-1.008)	-	7	
Freezing-point depression (°C)	-	(0.32-0.37)	-	2	
Surface tension (dyn cm ⁻¹)	-	(67-70)	-	12	Measured at 37-38 °C
Water (g/l)	-	(990-995)	-	2	
Dry substance (g/l)	-	(3-10)	-	7	Consists of 50% organic and 50% inorganic matter
pH value	-	(4-6.8)	-	6	Apocrine sweat is about 0.5 pH less acid than eccrine sweat ¹ , possibly because of its higher ammonia content ^{1,9}
Inorganic substances					
Chloride (mEq/l)					
(a) New born, 1st day	39	14-64	12.5	16	Measured on pilocarpine sweat from (a) 100, (b) 43, (c) 107, (d) 17, (e) 63 and (f) 31 subjects. On the method of determination see ¹⁷ On physiological and pathological changes in the chloride content of sweat see under "Sodium", page 680
(b) Children, 1-12 months	12.3	2.5-22.1	4.9	16	
(c) Children, 1-10 years	15.3	0-31.5	8.1	16	
(d) Children, 10-16 years	19.9	1.5-38.3	9.2	16	
(e) Adults, 17-50 years	29.7	0-65.1	17.7	16	
(f) Adults, over 50 years	38.9	34.3-43.5	2.3	16	
Phosphate (mg/l)	14	(10-17)	-	16	Measured on 4 children. Data on the phosphate content of sweat vary widely ⁷
Sulphate (mg/l)	-	(7-190)	-	7	Less than 50% is inorganic sulphate
Bromide (mg/l)	-	(0.182-0.502)	-	17	
Fluoride (mg/l)	-	(0.2-1.8)	-	20	
Iodine (µg/l)	9.5	(5.4-12.2)	-	21	Increased in cystic pancreatic fibrosis ²²

Eccrine sweat unless otherwise stated	Mean	95% range (extreme range in brackets)	s	Reference	Remarks
Potassium (mEq/l)					
(a) Newborn, 1st day	8	2-14	3	14	Measured in pilocarpine sweat from (a) 100, (b) 43, (c) 107, (d) 17, (e) (f) 6 subjects. The potassium content decreases slightly with increase of secretion ²⁴ . It is moderately increased in cystic pancreatic fibrosis ¹⁸ , but the change is not as characteristic as that in the sodium or chloride content.
(b) Children, 1-12 months . .	11.2	4.4-18.0	3.4	15	
(c) Children, 1-10 years	9.6	4.0-15.2	2.8	16	
(d) Children, 10-16 years . . .	8.5	3.7-13.3	2.4	15	
(e) Men, 20-60 years	7.5	4.3-10.7	1.6	23	
(f) Women, 20-60 years . . .	10.0	5.8-14.2	2.1	23	
Sodium (mEq/l)					
(a) Newborn, 1st day	36	10-62	13	14	Measured in pilocarpine sweat from (a) 100, (b) 43, (c) 107, (d) 17, (e) 33, and (g) 21 subjects. The amounts of sodium and chloride in sweat are dependent on many factors ²⁷ , such as hereditary disposition, age, season, sex, collection and diet; they increase as the rate of secretion increases and are higher in heat sweat than in pilocarpine sweat ¹⁸ . The sodium/chloride ratio is 1.0-1.37. In children and young adults the upper limit of the normal range of sodium concentration in heat sweat is reported to be 70-80 mEq/l corresponding figure for chloride being 60-70 mEq/l ^{11, 25, 27, 28} ; during first days of life this limit is somewhat higher ¹⁴ . In cystic pancreatic fibrosis the sodium and chloride contents of sweat almost always exceed these limits; a less characteristic increase in the sodium content is seen in malfunctioning of the adrenal cortex ⁶ (this can be corrected by giving aldosterone). The sodium and chloride contents are lowered in primary hyperaldosteronism ²⁹ .
(b) Children, 1-12 months . .	14.5	5.1-23.9	4.7	15	
(c) Children, 1-10 years	19.5	3.3-35.7	8.1	16	
(d) Children, 10-16 years . . .	29.2	6.0-52.4	11.6	15	
(e) Men, 20-60 years	51.9	9.7-94.1	21.1	23	
(f) Women, 20-60 years . . .	36.5	0-73.9	18.7	23	
(g) Adults, over 65 years . . .	55.5	7.5-104	24.0	26	
Calcium (mEq/l)	-	(0.2-6)	-	7	The calcium content increases with increasing rate of sweat secretion. Prolonged severe sweating may result in serious loss of calcium ³⁰ .
Magnesium (mEq/l)	-	(0.03-4)	-	7	
Iron (mg/l)					
Men	1.15	(0.63-1.88)	-	31	About 1/4 of the ingested iron is excreted in the sweat when this is free of the iron content of heat sweat from the arms being 190 µg/l, from the 250 µg/l ³² .
Women	1.61	(1.21-2.30)	-	32	
Copper (mg/l)	0.058	-	-	34	
Manganese (mg/l)	0.060	-	-	34	
Zinc (mg/l)	1.15	0.55-1.75	0.30	35	Heat sweat from 10 subjects.
Nitrogenous substances					
Total nitrogen (mg/l)	-	(230-400)	-	5	The nitrogen content of sweat varies widely, published values lying between 170 and 1960 mg/l, including 50-1500 mg/l urea-N, 10-350 mg/l ammonia and 10-100 mg/l amino-acid-N ⁷ .
Urea (mg/l)	-	(260-1220)	-	5	The urea content of sweat varies widely, published values lying between 100 and 2000 mg/l ¹⁸ ; in general it is about twice that of the serum ⁷ .
Creatinine (mg/l)	4.6	(2.1-8.4)	-	18	Values from heat sweat of 4 children. Published values range from 0 to 67 mg/l with a mean of about 4 mg/l ^{18, 7} .
Ammonia (mg/l)	-	(60-110)	-	5	The ammonia content of sweat varies widely, published values lying between 10 and 425 mg/l ⁷ ; this is partly due to differences in the extent to which urea is broken down by bacteria. It is 25-200 times greater than the ammonia content of the serum ⁷ .
Amino acids (g/l)					
(a) Children	1.40	1.23-1.58	0.087	18	(a) Calculated as leucine in the pilocarpine sweat of 18 children (in heat sweat the mean value is 2.65 g/l). (b) Heat sweat of 4 men. (c) Pilocarpine sweat of 151 men and women; the following were quantitatively determined (in order of decreasing concentration): citrulline, serine, glutamic acid, aspartic acid, arginine, threonine, alanine, leucine, glycine, histidine, ornithine, lysine, valine. Also detected in some samples were phenylalanine, tyrosine, proline, tryptophan, taurine.
(b) Adults	1.38	(0.54-2.59)	-	36	
(c) Adults	0.476	0.27-0.68	0.102	37	
Uric acid (mg/l)	-	(0-15)	-	5	Other studies ³⁸ found no uric acid in sweat.
Urocanic acid (mg/l)	57	1-113	28	18	Pilocarpine sweat of 18 children (mean value in heat sweat 148 mg/l).

The ejaculate (total semen) is a suspension of spermatozoa in a liquid medium, the seminal plasma. The latter consists of the various secretions of the accessory reproductive organs, namely the testes, epididymides, vasa deferentia, seminal vesicles, prostate and urethral and bulbo-urethral glands. The composition of the total semen depends on the amounts of these individual secretions contained in it. Those of the three principal fractions can be calculated from the content of acid phosphatase, characteristic of the prostate secretion, from the number of spermatozoa, characteristic of the testicular and epididymal secretions, and from the content of fructose, characteristic of the secretion of the seminal vesicles¹. The method of collection also has some effect on the composition.

In ejaculation a few drops of the urethral and bulbo-urethral

gland secretions are first discharged. This is followed by the prostate secretion, usually free of spermatozoa, then by the middle portion of the seminal vesical secretion containing the spermatozoa, and finally by the highly viscous part of the latter secretion². Immediately after ejaculation the semen coagulates as a result of the action of an enzyme from the prostate on a fibrinogen-like protein from the seminal vesicles. Within 15 minutes of ejaculation the semen liquefies as a result of fibrinolysis of the coagulum, a process involving a plasmin-like enzyme from the prostate; this is followed by hydrolysis of the proteins to amino acids and ammonia.

Unless otherwise stated, the data in the following table refer to the liquefied ejaculate. There is an extensive literature on the composition and properties of semen³⁻⁵.

Total semen unless otherwise stated	Mean	95% range (extreme range in brackets)	s	Reference	Remarks
Physicochemical data	For further data on spermatozoa see page 686.
Appearance	The fresh ejaculate is milky, slightly opalescent, and contains glassy, sticky threads as well as sago- and tapioca-like particles. The seminal vesical secretion occasionally contains yellow pigments (flavins).
Volume of the ejaculate (ml)	3.4	0.2-6.6	1.6	6	Values from 1000 measurements after continence of at least 3 days. Very variable in the same subject. Repeated coitus causes a reduction in the volume, long continence an increase (up to 13 ml). 13-33% of the ejaculate volume is from the prostate, 46-80% from the seminal vesicles, about 10% from the epididymides ^{1,3} .
Specific gravity	1.028	(1.020-1.040)	-	5, 7	The specific gravity of the whole ejaculate depends on the spermatozoal content.
	1.035	(1.031-1.039)	-	8	
Prostate secretion	1.022	(1.018-1.027)	-	8	
Seminal vesical secretion	1.037	-	-	8	
Freezing-point depression (°C)					
(a)	-	(0.56-0.58)	-	9	(a) 1 hour, (b) 16 hours after ejaculation.
(b)	-	(0.74-0.78)	-	9	
Osmolality (mosm/kg H₂O)					
Seminal plasma	296	-	-	10	
Spermatozoa	296	-	-	10	
Relative viscosity at 20 °C. ..	6.45	-	-	9	The viscosity of the whole ejaculate is largely dependent on the spermatozoal content; that of the prostate secretion is low, that of the seminal vesical secretion high. The ability to form threads is characteristic of the secretions of the urethral and bulbo-urethral glands ² .
Surface tension (dyn cm⁻¹)					
At 20 °C.	66	-	-	9	
At 15 °C.	-	(52-59.5)	-	11	
Specific conductivity (S cm⁻¹) at 20 °C.	-	(0.0088-0.0108)	-	9	
Water (g/l)	918	(891-944)	-	8	
Prostate secretion	932	(927-936)	-	8	
Seminal vesical secretion	890	-	-	8	
Spermatozoa (g/kg)	830	-	-	10	
Dry substance (g/l)	-	(80-130)	-	8	Consists of about 10% inorganic and 90% organic matter ^{1,2} .
pH value	7.19	(6.9-7.36)	-	8	Loss of CO ₂ on long standing causes semen to become alkaline (pH 7.6-8.0).
Prostate secretion	6.45	(6.3-6.6)	-	8	
Seminal vesical secretion	7.29	-	-	8	
Inorganic substances					
Carbon dioxide (mmol/l) ..	24	(19.2-33.2)	-	8	
Prostate secretion (mmol/l) ..	4.2	(3.1-5.4)	-	8	
Spermatozoa (mmol/kg)	10.5	-	-	10	
Chloride (mEq/l)	42.8	(28.3-57.3)	-	8	
Prostate secretion (mEq/l) ..	38.1	(34.8-46.1)	-	8	
Spermatozoa (mEq/kg)	33	-	-	10	

Semen

(For references see page 685)

Total semen unless otherwise stated	Mean	95% range (extreme range in brackets)	s	Reference	Remarks
Phosphorus (g/l)	1.12	—	—	5	The acid-soluble phosphorus of the seminal plasma consists mainly of phosphorylcholine and glycerylphosphorylcholine
Acid-soluble phosphorus ...	0.57	(0.28–0.94)	—	5	
Prostate secretion	0.03	(0.02–0.06)	—	12	
Seminal vesical secretion .	0.46	(0.30–0.62)	—	12	
Spermatozoa (g/kg) .. .	1.6	—	—	10	
Inorganic phosphorus	0.11	—	—	6	Increases on prolonged incubation at 37 °C as a result of progressive decomposition of proteins
Lipid phosphorus	0.06	—	—	5	
Potassium (mEq/l)	31.3	—	—	14	
	22.9	(17–27.4)	—	6	
Prostate secretion	48.3	(28.7–61.4)	—	6	
Seminal vesical secretion	17.8	—	—	6	Total of 19 free and peptide bound amino acids determined by column chromatography. All amino acids are present in considerably higher concentrations than in the blood plasma. 24 amino acids have been identified in semen by thin layer chromatography ²² .
Spermatozoa (mEq/kg) . . .	35	—	—	10	
Iodine (mEq/l)	117	(100–133)	—	6	
Prostate secretion	153	(149–158)	—	6	
Seminal vesical secretion	103	—	—	6	
Spermatozoa (mEq/kg) ..	110	—	—	10	2 minutes after ejaculation increases to more than 20 g/l 6 hours later as a result of liberation of choline from phosphorylcholine under the action of acid phosphatase
Calcium (mEq/l)	12.4	(10.6–14.3)	—	6	
Prostate secretion	60.4	(57.4–65.4)	—	6	
Seminal vesical secretion .	7	—	—	1	
Magnesium (mEq/l) .	11.5	—	—	6	
Copper (mg/l)	—	(0.06–0.24)	—	10	Total of 19 free and peptide bound amino acids determined by column chromatography. All amino acids are present in considerably higher concentrations than in the blood plasma. 24 amino acids have been identified in semen by thin layer chromatography ²² .
Zinc (mg/g dry substance)	—	—	—	10	
Seminal plasma	3.1	—	—	10	
Prostate secretion	7.2	—	—	12	
Spermatozoa	2.0	—	—	10	
Nitrogenous substances					
Total nitrogen (g/l)	9.13	(5.60–12.25)	—	6	Total of 19 free and peptide bound amino acids determined by column chromatography. All amino acids are present in considerably higher concentrations than in the blood plasma. 24 amino acids have been identified in semen by thin layer chromatography ²² .
Prostate secretion	4.16	(2.95–5.11)	—	6	
Seminal vesical secretion	12.84	(12.33–13.43)	—	6	
Nonprotein nitrogen (g/l)	0.96	(0.73–1.30)	—	6	
Prostate secretion	0.54	(0.30–0.90)	—	6	
Seminal vesical secretion	0.99	—	—	6	2 minutes after ejaculation increases to more than 20 g/l 6 hours later as a result of liberation of choline from phosphorylcholine under the action of acid phosphatase
Ammonia (mg/l)	20	—	—	1	
Urea (mg/l)	—	—	—	19	
Seminal plasma	720	—	—	19	
Creatine (mg/l)	—	—	—	20	
Seminal plasma	170	—	—	20	2 minutes after ejaculation increases to more than 20 g/l 6 hours later as a result of liberation of choline from phosphorylcholine under the action of acid phosphatase
Arginine (mg/l)	—	—	—	20	
Seminal plasma	900	—	—	20	
Amino acids (g/l)	—	—	—	20	
Seminal plasma	12.6	—	—	20	
Choline (free) (g/l)	0.70	—	—	23	2 minutes after ejaculation increases to more than 20 g/l 6 hours later as a result of liberation of choline from phosphorylcholine under the action of acid phosphatase
Phosphorylcholine (g/l)	3.06	(2.86–3.80)	—	24	
Glycerylphosphorylcholine (g/l)	0.66	(0.54–0.90)	—	24	

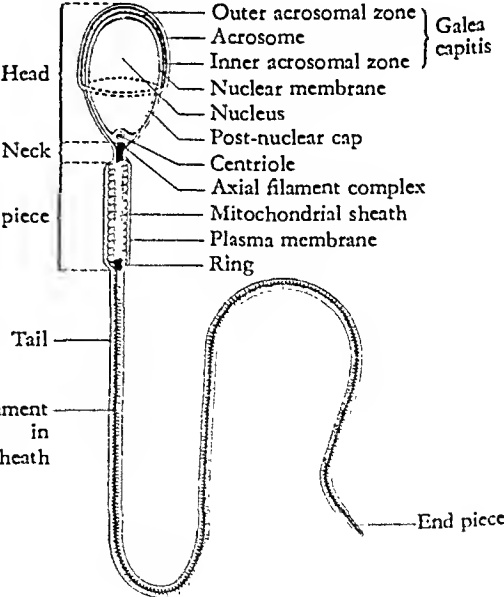
Amount which differs otherwise stated	Mean	(extreme range in brackets)	r	Reference	Remarks
Spermine (g/l)	—	(0.5–3.5)	—	5	Includes about 10% of the diamines spermidine, 1,3-propanediamine and putrescine ²⁵ .
Ergothioneine (mg/l)					
Seminal plasma	15	—	—	26	
Seminal vesical secretion	—	(<10)	—	5	
Glutathione (mg/l)					
Seminal plasma	300	—	—	27	
Uric acid (mg/l)	60	—	—	5	
Proteins (g/l) (a)	45.0	(32.9–68.5)	—	8	(a) (Total nitrogen – nonprotein nitrogen) × 6.25; (b) determined gravimetrically; (c) determined by biuret reaction. As immunoelectrophoretic studies ^{28–30} have shown, the seminal plasma contains various serum proteins (albumin, α_1 -globulin, α_2 -globulin, transferrin and γ G-globulin) as well as organ-specific proteins arising partly from the prostate ^{29,31} , partly from the seminal vesicles ²⁹ . After ejaculation the seminal proteins are rapidly broken down by the action of proteolytic enzymes. The proteins of the spermatozoa consist mainly of nucleoproteins and enzymes.
(b)	58.0	(43.0–77.4)	—	8	
Seminal plasma (c)	—	(18–47)	—	28	
Prostate secretion (a)	21.7	(16.6–29.3)	—	8	
(b)	25.5	(24.6–26.4)	—	8	
Seminal vesical secretion (a)	77.8	—	—	8	
(b)	90.4	—	—	8	
Mucoproteins (g/l)					
Seminal plasma	9	—	—	32	The semen probably also contains other mucoproteins in addition to this fraction adsorbable on benzoic acid.
Sialic acid (g/l)	—	(0.60–1.05)	—	33	Only about 4% of this is dialysable ³⁴ , indicating that the sialic acid is a component of the mucoproteins.
Prostate secretion	—	(0.75–1.05)	—	33	
Seminal vesical secretion	—	(<1.3)	—	33	
Deoxyribonucleic acid (pg per spermatozoal nucleus)	2.5	—	—	35	The amount of DNA, an integral component of the chromosomes, in the spermatozoa of men of normal fertility is constant and fairly uniform, whereas in those of men with doubtful fertility it is inconstant and varies widely from one individual to another ^{35,36}
Enzymes	The spermatozoa are rich in various enzymes ⁵ such as cytochromes, succinate dehydrogenase, lactate dehydrogenase, malate dehydrogenase and adenosine triphosphatase. The spermatozoal head contains hyaluronate lyase lightly bound to the cell surface and readily released into the seminal fluid. The seminal plasma contains many enzymes; quantitatively determined have been lactate dehydrogenase ³⁷ , malate dehydrogenase ³⁷ , isocitrate dehydrogenase ³⁷ , glutathione reductase ³⁷ , aspartate aminotransferase ³⁸ , alanine aminotransferase ³⁸ , creatine kinase ³⁹ , phosphatases ⁴⁰ , α -glucosidase ⁴¹ , β -galactosidase ⁴² , α -mannosidase ⁴² , β -mannosidase ⁴² , chitinase ⁴² , β -glucuronidase ⁴² . The seminal plasma has a high fibrinolytic and proteolytic activity ⁵ but the enzymes responsible have not been clearly identified.
Alkaline phosphatase (U/l, 37 °C)					
Seminal plasma	—	(18–177)	—	40	For definition of the unit U see page 584.
Acid phosphatase (kU/l, 37 °C)					
Seminal plasma	—	(96–750)	—	40	For definition of the unit U see page 584. The acid phosphatase of semen arises mainly from the prostate. The phosphatase content is fairly constant in different ejaculates of the same individual but may vary widely in different individuals
Prostate secretion					
Boys, 11 years	9	—	—	43	
Boys, 16 years	1540	—	—	43	
Men, 20–40 years	2560	—	—	44	
Men, 40–100 years	660	—	—	44	
Non-nitrogenous substances					
Fructose (g/l)	2.24	(0.91–5.20)	—	5	The fructose content of semen arises mainly from the seminal vesicles and varies widely. None is detectable before puberty or after castration. Values below 1.2 g/l indicate impaired functioning of the interstitial cells of Leydig.
Seminal vesical secretion	3.15	(1.7–8.2)	—	7, 5	
Glycogen (g/l)					
Seminal plasma	—	(0.14–5.5)	—	41	
Inositol (g/l)					
Seminal plasma	0.6	—	—	45	

Total semen unless otherwise stated	Mean	95% range (extreme range in brackets)	s	Reference	Remarks
Sorbitol (g/l)					
Seminal plasma	0.1	—	—	46	
Pyruvic acid (g/l)					
Seminal plasma	0.29	(0.11–0.56)	—	37	
Citric acid (g/l)	3.76	(0.96–14.3)	—	8	The citric acid content of the semen is a measure of androgenic activity, that of the prostate secretion gradually diminishes after castration
Prostate secretion	—	(4.80–26.9)	—	8	
Seminal vesical secretion	—	(0.15–0.22)	—	8	
Lactic acid (g/l)	0.37	(0.28–0.52)	—	1	
Prostate secretion	0.50	—	—	1	
Lipids					
Total lipids (g/l)					
Seminal plasma	1.88	(1.67–2.06)	—	47	The spermatozoa are rich in various lipids ⁴⁸ (lipoproteins, triglycerides, free fatty acids, sterols, phospholipids — particularly acetalphosphatides — heptacosan). The lipids of the seminal plasma arise mainly from the prostate and are partly contained in the formed elements of the secretion
Prostate secretion	2.86	(2.60–3.10)	—	47	
Phospholipids (g/l)					
Seminal plasma	0.84	(0.48–1.33)	—	47	
Prostate secretion	1.80	(1.44–2.25)	—	47	
Cholesterol (g/l)					
Seminal plasma	1.03	(0.70–1.20)	—	47	
Prostate secretion	0.80	(0.62–1.05)	—	47	
Prostaglandins (mg/l)					
Seminal plasma					Primary prostaglandins: PGE compounds 53.5 mg/l, PGF compounds 8 mg/l, also metabolites of PGE compounds 250 mg/l ⁴⁹
Vitamins					
Tocopherol (mg/kg)	9.8	—	—	49	
Vitamin B ₁₂ (μg/l)					
Seminal plasma	—	(0.30–0.60)	—	50	Determined with <i>Escherichia gracilis</i> . Values are from semen with morphologically normal spermatozoa
Ascorbic acid (mg/l)	43	(18–72)	—	51	The ascorbic acid probably arises from the seminal vesicles rather than from the prostate ⁵²

References (pages 682–685)

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³ JENSEN, K., in FLÄSCHENBÄCKER and LEHNHART (Eds.), *Physiologische Chemie*, vol. 2, part 2b, Springer, Berlin, 1954, page 563

⁴⁸ DAWSON et al., *Biochem J.*, 65, 627 (1957).

	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Remarks
Number (millions/ml)					
(a)	106.6	0-256	74.5	¹	(a) 1000 measurements. The spermatozoal concentration may vary widely in the same individual and is depressed particularly by emotional excitement and physical effort. In some cases long continence also lowers the concentration (but increases the proportion of abnormal forms), as does too high a testicular temperature (cause of testicular degeneration in cryptorchism). Seasonal variations have also been observed (diminished spermatozoal concentration during the warm months) but are not statistically significant. There is no absolute correlation between spermatozoal concentration and fertility or infertility, but in general the spermatozoal content of the ejaculate is lower in infertile men. To this may be added an absolute reduction in the number of spermatozoa due to a smaller volume of the ejaculate, or a dilution of the spermatozoa when the volume of the ejaculate is excessive. The minimum spermatozoal concentration for a fertile semen is regarded as 20-25 million/ml ² .
(b)	-	(28-225)	-	²	
Spermatozoal (ml sperma- tozoa/l semen)	~10	-	-	⁴	
Electrophoretic mobility (10⁻⁸ cm² s⁻¹ V⁻¹)	-	(6.1-8.7)	-	⁵	At pH 7.8 and 20 °C. The spermatozoa migrate to the anode.
Motility					
In vitro (s mm ⁻¹)	-	(40-50)	-	⁵	Normokinetic spermatozoa maintain their motility even 12 hours after ejaculation ⁶ . In the female genital tract motility is probably maintained for 48 hours. Spermatozoa can be classified according to their motility as follows ¹¹ : 1. Nonmotile (dead), 15%; 2. only slightly motile, 15%; 3. moderately and 4. very motile, together at least 75%. A fertile semen should contain at least 40-60% of normally motile spermatozoa ³ .
In vitro (mm min ⁻¹)	-	(0.3-0.6)	-	⁷	
In vivo (mm min ⁻¹)	-	(1.3-2.6)	-	⁷	
Spermatozoal forms (%)					
Oval	89.8	(66-99)	-	⁸	A fertile semen should contain at least 60% of morphologically normal spermatozoa and not more than 10% of spermiocytogenic cells ⁹ .
Tapering	3.6	(0-24)	-	⁸	
Round	1.6	(0-9)	-	⁸	
Duplicate	1.8	(0-11)	-	⁸	
Giant and pinhead	0.6	(0-8)	-	⁸	
Amorphous	2.1	(0-12)	-	⁸	
Spermatozoal dimensions					
Weight (pg)	37	-	-	⁹	Diagram of the human spermatozoon¹⁰
Head					
Length (μm)	4.4	(3.3-6.2)	-	⁹	
Width (μm)	3.2	-	-	⁹	
Thickness (μm)	2.0	-	-	⁹	
Volume (μm ³)	6.4	-	-	⁹	
Middle piece					
Length (μm)	4.0	-	-	⁹	Axial filament in fibrous sheath
Diameter (μm)	1.0	-	-	⁹	
Volume (μm ³)	3.1	-	-	⁹	
Tail					End piece
Length (μm)	-	(40-60)	-	⁹	
Diameter (μm)	-	(0.4-0.7)	-	⁹	
Volume (μm ³)	-	(4.5-6.8)	-	⁹	
End piece					
Length (μm)	-	(6-10)	-	⁹	
Diameter (μm)	0.2	-	-	⁹	
Volume (μm ³)	0.16	-	-	⁹	

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- ¹⁰ Modified from MANN, T., *The Biochemistry of Semen and of the Male Reproductive Tract*, Methuen, London, 1964, page 20.
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m

In general the yield corresponds to the needs of the infant, amounting to about 850 ml per day for a body weight of 5-6 kg.

imposition (see pages 688 and 689)

It is easy to obtain some milk for chemical analysis, and many

course of the day.² For example, the fat content of milk rises

The daily variation in composition mainly concerns the fat content.² In one study² this was usually lowest at 6 a.m., highest

times must be carefully standardized if valid comparisons are made between subjects.²

The collection of a 24-hour milk sample means removing the child from the breast during that time and emptying the breast preferably by pump. The administrative difficulties involved some workers to leave the child on one breast while the contents of the other. But even this may mislead, the variation of milk from the two breasts is not necessarily the same.

There is no escape from the necessity of obtaining composite hour samples from both breasts if misleading measurements are to be avoided. But since this is seldom done, comparisons of milk analyses reported in the literature must be made with utmost caution.

The composition of breast milk is described in detail by MACY and KELLY² and LINTZEL.² Data have also been published by the Committee on Nutrition of the American Academy of Pediatrics.¹⁰

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Fatty acids (as percentage by weight of total fatty acids)*

	Mature milk			Colostrum 3rd day			Colostrum 2nd day			Colostrum 1st day			Cow's milk	
	Mean	s	Reference	Mean	s	Reference	Mean	s	Reference	Mean	s	Reference	Mean	s
Butyric acid	0.4	-	1	0.3	-	1	0.2	-	1	0.2	-	1	2.7	0.5
Caproic acid	0.1	0.1	2	0.1	-	1	0.1	-	1	0.1	-	1	2.0	0.2
Caprylic acid	0.1	0.2	2	0.1	-	1	0.1	-	1	0.1	-	1	1.2	0.2
Capric acid	0.8	0.4	2	0.9	-	1	0.8	-	1	0.8	-	1	3.2	0.7
Myristic acid	4.7	2.2	2	2.5	1.1	1	3.5	-	1	3.5	-	1	3.6	1.1
Palmitic acid	7.9	1.5	2	5.7	1.7	1	3.6	1.3	1	3.7	1.3	1	11.8	1.5
Stearic acid	26.7	2.7	2	26.1	3.0	1	26.1	2.7	1	26.9	2.8	1	36.6	4.7
Arachidic acid	8.5	1.7	2	5.8	0.9	1	6.5	1.4	1	7.0	1.0	1	8.1	3.2
Docosanoic acid	1.3	-	2	-	-	1	-	-	1	-	-	1	1.7	-
Tricosanoic acid	0.1	-	1	0.1	-	1	0.2	-	1	0.2	-	1	0.3	-
Stearic acid	0.1	-	1	0.1	-	1	0.1	-	1	0.1	-	1	0.2	-
Palmitoleic acid	0.24	-	2	0.2	-	1	0.1	-	1	0.1	-	1	1.5	-
Oleic acid	3.4	1.0	2	5.4	0.8	1	4.4	1.5	1	4.3	1.6	1	3.2	0.7
Eicosenoic acid	37.4	5.7	2	43.1	4.5	1	44.2	3.4	1	44.0	4.4	1	17.7	4.6
Linoleic acid	0.89	-	1	-	-	1	-	-	1	-	-	1	1.0	-
Linolenic acid	10.6	2.9	2	9.0	1.8	1	11.4	1.7	1	11.9	3.0	1	2.1	0.7
Arachidonic acid	0.85	-	2	0.3	-	1	0.3	-	1	0.3	-	1	1.7	0.7
	0.57	-	2	1.6	-	1	1.6	-	1	1.8	-	1	0.4	-

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- ¹⁰ PEARSON and MACARTHY, *Am J Clin Nutr*, **8**, 377 (1960)

	Mean	95% range (extreme range in brackets)	<i>s</i>	Refer- ence	Remarks
Number (millions/ml)					
.....	106.6	0-256	74.5	¹	(a) 1000 measurements. The spermatozoal concentration may vary widely in the same individual and is depressed particularly by emotional excitement and physical effort. In some cases long continence also lowers the concentration (but increases the proportion of abnormal forms), as does too high a testicular temperature (cause of testicular degeneration in cryptorchism). Seasonal variations have also been observed (diminished spermatozoal concentration during the warm months) but are not statistically significant. There is no absolute correlation between spermatozoal concentration and fertility or infertility, but in general the spermatozoal content of the ejaculate is lower in infertile men. To this may be added an absolute reduction in the number of spermatozoa due to a smaller volume of the ejaculate, or a dilution of the spermatozoa when the volume of the ejaculate is excessive. The minimum spermatozoal concentration for a fertile semen is regarded as 20-25 million/ml ² .
.....	-	(28-225)	-	²	
Matocrit (ml spermatozoa/ml semen)	~10	-	-	⁴	
Trophoretic mobility (10^{-5} cm ² s ⁻¹ V ⁻¹)	-	(6.1-8.7)	-	⁵	At pH 7.8 and 20 °C. The spermatozoa migrate to the anode.
Motility					
Total (s mm ⁻¹)	-	(40-50)	-	⁶	Normokinetic spermatozoa maintain their motility even 12 hours after ejaculation ⁶ . In the female genital tract motility is probably maintained for 48 hours. Spermatozoa can be classified according to their motility as follows ⁷ : 1. Nonmotile (dead), 15%; 2. only slightly motile, 15%; 3. moderately and 4. very motile, together at least 75%. A fertile semen should contain at least 40-60% of normally motile spermatozoa ³ .
Total (mm min ⁻¹)	-	(0.3-0.6)	-	⁷	
Vigilant (mm min ⁻¹)	-	(1.3-2.6)	-	⁷	
Vigilant (mm min ⁻¹)	-	(1.3-2.6)	-	⁷	
Spermatozoal forms (%)					
.....	89.8	(66-99)	-	⁸	A fertile semen should contain at least 60% of morphologically normal spermatozoa and not more than 10% of spermiocytogenic cells ³ .
.....	3.6	(0-24)	-	⁸	
.....	1.6	(0-9)	-	⁸	
.....	1.8	(0-11)	-	⁸	
.....	0.6	(0-8)	-	⁸	
.....	2.1	(0-12)	-	⁸	
Spermatozoal dimensions					
Height (μg)	37	-	-	⁹	<p>Diagram of the human spermatozoon¹⁰</p>
Length (μm)	4.4	(3.3-6.2)	-	⁹	
Width (μm)	3.2	-	-	⁹	
Thickness (μm)	2.0	-	-	⁹	
Volume (μm ³)	6.4	-	-	⁹	
Middle piece					
Length (μm)	4.0	-	-	⁹	
Diameter (μm)	1.0	-	-	⁹	
Volume (μm ³)	3.1	-	-	⁹	
Tail					
Length (μm)	-	(40-60)	-	⁹	
Diameter (μm)	-	(0.4-0.7)	-	⁹	
Volume (μm ³)	-	(4.5-6.8)	-	⁹	
End piece					
Length (μm)	-	(6-10)	-	⁹	
Diameter (μm)	0.2	-	-	⁹	
Volume (μm ³)	0.16	-	-	⁹	

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¹¹ WEISMAN, A. I., *Spermatozoa and Sterility*, Hoeber, New York, 1941.

	Mature milk (15 days to 15 months post partum)				Transitional milk (6-10 days post partum)				Colostrum (first 5 days post partum)				Cow's milk			
	Mean	Experimen- tal range	s	Refer- ence	Mean	Experimen- tal range	s	Refer- ence	Mean	Experimen- tal range	s	Refer- ence	Mean	Experimen- tal range	s	Refer- ence
Calories																
kcal/l)	747	446-1192	93	1	735	678-830	36	1	671	588-730	-	1	701	587-876	-	2
kJ/l)	3.127	1.867-4.989	0.389	Ed	3.076	2.838-3.474	0.151	Ed	2.808	2.461-3.055	-	Ed	2.934	2.457-3.666	-	Ed
Specific gravity	1.031	1.026-1.037	0.002	1	1.035	1.034-1.036	-	1	1.034	-	-	3e	1.031	1.028-1.033	-	3
pH	7.01	6.4-7.6	-	4	-	-	-	-	-	-	-	-	6.6	-	-	5
Solids, total (g/l)	129	103-175	11	1	133	105-156	8	1	128	100-167	13	1	124	119-142	-	3
Ash, total (g/l)	2.02	1.6-2.66	0.18	1	2.67	2.31-3.38	0.32	1	3.08	2.47-3.50	-	1	7.15	6.81-7.71	-	6
Minerals																
(a) Electropositive elements (mEq/l)	41	-	-	1	55	-	-	1	68	-	-	1	149	-	-	Ed
Sodium (g/l)	0.172	0.064-0.436	0.045	1	0.294	0.192-0.539	0.076	1	0.501	0.265-1.37	0.28	1	0.768	0.392-1.39	-	7
Potassium (g/l)	0.189	0.080-0.350	0.066	39	0.536	0.170-1.21	0.271	39	0.956	0.330-2.24	0.377	39	-	-	-	-
Calcium (g/l)	0.512	0.373-0.635	0.085	1	0.636	0.528-0.769	0.068	1	0.745	0.658-0.870	-	1	1.43	0.38-2.87	-	8
Magnesium (g/l)	0.553	0.425-0.735	0.070	39	0.692	0.450-0.910	0.099	39	0.581	0.220-0.790	0.120	39	-	-	-	-
Phosphorus (g/l)	0.344	0.173-0.609	0.067	1	0.464	0.23-0.628	0.095	1	0.481	0.242-0.656	0.121	1	1.37	0.56-3.81	-	8
Sulphur (g/l)	0.271	0.207-0.372	0.030	39	0.320	0.166-0.420	0.045	39	0.261	0.180-0.364	0.026	39	-	-	-	-
Chlorine (g/l)	0.035	0.018-0.057	0.007	1	0.035	0.026-0.054	0.006	1	0.042	0.031-0.082	0.013	1	0.13	0.07-0.22	-	8
(b) Electronegative elements (mEq/l)	28	-	-	1	37	-	-	1	40	-	-	1	108	-	-	Ed
Phosphorus (g/l)	0.141	0.068-0.268	0.025	1	0.198	0.097-0.317	0.047	1	0.157	0.085-0.251	0.047	1	0.91	0.56-1.12	-	8
Sulphur (g/l)	0.14	0.05-0.30	0.03	1	0.20	0.15-0.23	0.02	1	0.23	0.20-0.26	-	1	0.30	0.24-0.36	-	8
Chlorine (g/l)	0.375	0.088-0.734	0.09	1	0.457	0.305-0.721	0.109	1	0.586	0.435-1.01	-	1	1.08	0.93-1.41	-	8
(c) Excess electropositive elements (mEq/l)	13	-	-	1	18	-	-	1	28	-	-	1	41	-	-	Ed
(d) Trace elements																
Cobalt (μg/l)	trace	-	-	-	-	-	-	-	-	-	-	-	0.6	-	-	9
Iron (mg/l)	0.50	0.20-0.80	-	10	0.59	0.29-1.45	-	40	1.0	-	-	11	0.45	0.25-0.75	-	10
Copper (mg/l)	0.51	-	0.046	11	1.04	-	0.073	11	1.34	-	0.112	11	0.102	-	-	11
Manganese (mg/l)	trace	-	-	12	trace	-	-	13	trace	-	-	13	0.02	0.005-0.067	-	14
Zinc (mg/l)	1.18	0.17-3.02	-	8	3.82	0.39-5.88	-	8	5.59	0.72-9.81	-	8	3.9	1.7-6.6	-	8
Fluorine (mg/l)	0.107	0.0-0.24	-	15	-	-	-	-	0.131	0.0-0.35	-	15	-	0.10-0.28	-	16
Iodine (mg/l)	0.061	0.044-0.093	-	17	-	-	-	-	-	0.045-0.450	-	18	0.116	0.036-1.05	-	17
Selenium (mg/l)	0.021	-	-	41	-	-	-	-	-	-	-	-	0.04	0.005-0.067	-	41
Protein																
Total (g/l)	10.6	7.3-20	4.6	1	15.9	12.7-18.9	9.8	1	22.9	14.6-68.0	12.6	1	32.46	28.16-36.76	-	18
Casein (g/l)	3.7	1.4-6.8	0.8	1	5.1	4.2-5.9	-	1	55	14-215	-	20	-	-	-	-
Whey protein* (g/l)	7	4-10	-	21	-	-	-	1	21	7.3-52	-	20	24.9	21.9-28.0	-	19
'Lactalbumin' (g/l)	3.6	1.4-6.0	1.0	1	7.8	6.9-8.6	-	1	-	-	-	7	-	6-10	-	21
'Lactoglobulin' (g/l)	-	-	-	-	5.0	2.1-13.6	-	20	35	4.2-133	-	20	1.7	1.4-3.3	-	19
Blood-serum albumin (g/l)	0.32	0.20-0.47	-	22	0.37	0.26-0.65	-	22	2.5	-	-	42	0.4	0.7-3.7	-	43
Blood-serum immuno- globulin (g/l)	0.09	0.02-0.27	-	22	0.36	0.01-0.96	-	22	1.0	-	-	42	0.8	-	-	43
Amino acids																
Total (g/l)	12.8	9.0-16.0	-	23	9.4	6.0-10.0	-	23	12.0	7.0-40.0	-	23	33.0	27.0-41.0	-	23
Alanine (g/l)	-	0.36-0.42	-	24	-	-	-	-	-	-	-	-	0.75	-	-	44
Arginine (g/l)	0.43	0.28-0.64	0.088	1	0.63	0.48-0.73	0.069	1	0.74	0.62-0.96	-	1	1.4	1.2-1.6	-	25
Aspartic acid (g/l)	-	0.89-0.98	-	24	-	-	-	-	-	-	-	-	1.7	-	-	44
Cystine (g/l)	-	0.23-0.25	-	24	-	-	-	-	-	-	-	-	-	-	-	44
Glutamic acid (g/l)	-	1.89-2.00	-	24	-	-	-	-	-	-	-	-	6.8	-	-	44
Glycine (g/l)	-	0.23-0.24	-	24	-	-	-	-	-	-	-	-	0.11	-	-	44
Histidine (g/l)	0.24	0.12-0.30	0.041	1	0.38	0.29-0.45	0.046	1	0.41	0.35-0.46	-	1	1.2	1.1-1.3	-	25
Isoleucine (g/l)	0.61	0.41-0.92	0.121	1	0.97	0.73-1.21	0.110	1	1.01	0.88-1.15	-	1	2.5	2.1-2.9	-	25
Leucine (g/l)	0.97	0.65-1.47	0.174	1	1.51	1.13-1.97	0.219	1	1.66	1.33-2.14	-	1	3.6	3.2-3.9	-	25
Lysine (g/l)	0.70	0.36-0.93	0.127	1	1.13	0.88-1.48	0.157	1	1.18	0.95-1.41	-	1	2.6	2.3-3.1	-	25
Methionine (g/l)	0.12	0.07-0.16	0.023	1	0.24	0.16-0.34	0.040	1	0.25	0.19-0.36	-	1	0.8	0.6-0.9	-	25
Phenylalanine (g/l)	0.40	0.24-0.58	0.069	1	0.62	0.48-0.71	0.062	1	0.70	0.60-0.84	-	1	1.8	1.5-2.2	-	44
Proline (g/l)	-	0.84-0.94	-	24	-	-	-	-	-	-	-	-	2.5	-	-	44
Serine (g/l)	-	0.47-0.51	-	24	-	-	-	-	-	-	-	-	1.6	-	-	25
Threonine (g/l)	0.52	0.30-0.66	0.085	1	0.78	0.61-0.91	0.079	1	0.85	0.75-1.04	-	1	1.7	1.3-2.2	-	25
Tryptophan (g/l)	0.19	0.14-0.26	0.030	1	0.28	0.23-0.32	0.024	1	0.32	0.25-0.42	-	1	0.6	0.4-0.8	-	25
Tyrosine (g/l)	-	0.46-0.52	-	24	-	-	-	-	-	-	-	-	-	-	-	-
Valine (g/l)	0.73	0.45-1.14	0.155	1	1.05	0.77-1.36	0.122	1	1.17	0.98-1.49	-	1	2.6	2.4-2.8	-	25
Nonprotein nitrogen																
Total (g/l)																

Weight gain in pregnancy (per 4-week period)¹

4-week period of pregnancy	USA 1940 ²		England 1957 ³		India 1959 ⁴		Desirable gain ⁵		4-week period of pregnancy	USA 1940 ²		England 1957 ³		India 1959 ⁴		Desirable gain ⁵	
	lb	kg	lb	kg	lb	kg	lb	kg		lb	kg	lb	kg	lb	kg	lb	kg
12-16	3.5	1.6	3.1	1.4	2.0	0.9	2.4	1.1	29-32	4.0	1.8	3.3	1.5	2.0	0.9	4.4	2.0
17-20	5.1	2.3	4.2	1.9	2.4	1.1	2.9	1.3	33-36	4.0	1.8	3.5	1.6	1.8	0.8	4.4	2.0
21-24	5.1	2.3	4.6	2.1	3.3	1.5	3.3	1.5	37-40	3.3	1.5	3.3	1.5	0.7	0.3	2.6	1.2
25-28	4.6	2.1	4.2	1.9	2.0	0.9	4.2	1.9									

¹ For other values see HYTTEN and LEITCH, *The Physiology of Human Pregnancy*, Blackwell, Oxford, 1964, page 214.

² STANDER and PASTORE, *Amer. J. Obstet. Gynec.*, 39, 928 (1940) (2324 subjects).

³ THOMSON and BILLEWICZ, *Brit. med. J.*, 1, 243 (1957) (2868 subjects).

⁴ VENKATACHALAM et al., *Indian J. med. Res.*, 48, 511 (1960) (130 subjects).

⁵ HÜTER et al., *Geburtsh. u. Frauenheilk.*, 25, 385 (1965). According to these workers, the gain in weight in healthy women (overall mean 10.2 kg) is independent of age, body size and parity.

Weight gain in pregnancy (per week) from a study on primigravidae made in the Aberdeen Maternity Hospital between 1950 and 1955 (P = percentile)

Weeks of pregnancy	Number	80 %									
		50 %									
		P ₁₀		P ₂₅		P ₅₀		P ₇₅		P ₉₀	
		lb	kg	lb	kg	lb	kg	lb	kg	lb	kg
13-20	2868	0.42	0.19	0.64	0.29	0.93	0.42	1.19	0.54	1.45	0.66
20-30	2868	0.60	0.27	0.90	0.41	1.06	0.48	1.32	0.60	1.59	0.72
30-36	2868	0.35	0.16	0.62	0.28	0.93	0.42	1.28	0.58	1.59	0.72
36-40	2868	0.04	0.02	0.42	0.19	0.82	0.37	1.24	0.56	1.43	0.65
20-term (39, 40 or 41 weeks)*	486	0.31	0.14	0.75	0.34	0.97	0.44	1.24	0.56	1.50	0.68

* Group aged 20-29 years, healthy, no major clinical abnormality.

¹ HYTTEN and LEITCH, *The Physiology of Human Pregnancy*, Blackwell, Oxford, 1964, page 214; HYTTEN, F. E., personal communication.

Analysis of weight gain in pregnancy (some values are estimates)¹

Weeks of pregnancy	Whole body	Foetus	Placenta	Amniotic fluid	Uterus	Breasts	Plasma	Erythrocytes	Extra-cellular, extra-vascular water
Total weight gain (g)									
10	650	5	20	30	135	34	100		0
20	4000	300	170	250	585	180	600		0
30	8500	1500	430	600	810	360	1300		0
40	12500	3300	650	800	900	405	1250		1200
Protein storage (g)									
10	35	0.3	2	0	23	9	0		-
20	210	27	16	0.5	100	36	30		-
30	535	160	60	2	139	72	102		-
40	910	435	100	3	154	81	137		-
Fat storage (g)		Insignificant	Insignificant	-	0.5	1.4	0.4	-	-
10	367								
20	1930	2	1	-	2.3	5.4	3.9	-	-
30	3613	80	3	-	3.2	10.8	17.4	-	-
40	4464	430	4	-	3.6	12.2	19.6	-	-
Gain in water (ml)									
40	7000	2343	540	792	743	304	920	163	1195
Gain in extracellular water (ml)									
40	5165	1360	260	792	490	148	920	0	1195
Gain in intracellular water (ml)									
40	1835	983	280	0	253	156	0	163	0
Sodium storage (mEq)									
40	850	280	57	100	78	35	140	5	155
Potassium storage (mEq)									
40	316	154	42	3	49	35	4	24	5
Calcium storage (g)									
40	29.6	28.0	0.65	Insignificant	0.22	0.06	0.12	0.38	0.15

¹ HYTTEN and LEITCH, *The Physiology of Human Pregnancy*, Blackwell, Oxford, 1964.

and lipid contents of the plasma before, during and after pregnancy (g/l)¹

	Number	Albumin		α_2 -Globulin		β -Globulin		γ -Globulin		Fibrinogen		Total lipids	
		Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s
pregnant women.....	17	38.3	2.7	5.9	0.98	8.8	1.3	14.1	2.4	3.6	0.85	6.2	0.74
1st women (weeks)	15	32.6	2.8	6.8	1.3	9.4	1.0	16.1	2.7	3.9	0.7	5.9	1.0
.....	23	30.1	3.2	7.0	1.3	10.0	1.8	15.5	2.3	4.5	0.7	5.7	1.2
.....	22	28.7	3.8	7.6	1.2	9.6	1.8	15.2	2.8	4.3	0.8	6.1	1.2
.....	16	25.3	2.8	7.8	1.5	10.8	1.7	13.7	2.0	4.8	1.0	7.8	1.7
.....	22	25.9	3.0	7.4	1.2	11.0	1.5	14.7	2.7	5.1	1.2	8.1	1.4
.....	22	23.3	2.6	7.1	1.1	10.6	1.4	14.4	2.4	4.5	0.9	8.7	1.3
.....	18	24.8	2.7	6.5	1.0	11.0	1.6	13.3	3.6	4.6	1.0	8.8	1.3
.....	15	22.9	2.8	7.3	1.0	10.6	1.5	13.7	1.8	5.0	1.1	9.4	1.8
.....	20	23.5	3.0	7.5	1.0	11.7	1.5	14.1	2.4	5.3	1.1	9.5	1.2
.....	24	23.0	2.2	7.7	1.1	11.9	1.5	14.1	2.3	5.2	1.5	10.0	1.4
.....	21	23.7	2.8	7.3	1.1	11.0	1.4	14.0	2.0	5.3	1.4	10.0	1.0
.....	18	24.0	3.3	7.4	1.0	12.0	1.6	13.6	2.8	5.8	1.3	9.0	1.4
1st women (months)	15	21.6	2.5	7.1	1.0	10.1	1.7	14.1	2.0	5.0	1.0	8.6	1.1
.....	36	20.3	3.2	7.3	1.0	10.4	1.6	13.3	3.0	5.5	1.9	9.2	2.0
.....	26	21.0	2.9	7.4	1.2	10.5	1.5	13.9	2.2	5.9	1.4	8.9	1.3
.....	16	22.1	2.5	7.7	1.1	10.8	1.4	12.3	3.5	5.7	1.6	9.1	1.0
.....	40	22.9	3.3	8.5	1.7	11.6	1.5	15.3	3.4	6.1	1.9	9.4	2.0
.....	32	25.2	2.8	9.1	1.3	12.1	1.6	16.6	2.9	6.0	1.6	9.1	1.7
.....	10	26.2	1.7	9.0	2.1	11.6	1.2	17.1	3.6	6.0	2.1	8.3	1.1
.....	13	33.3	3.0	6.8	1.2	9.1	1.6	17.8	3.7	3.8	0.8	6.6	1.1

o et al, *Amer J Obstet Gynec*, 86, 820 (1963)

values in pregnancy¹

	Plasma volume (ml)	Erythrocyte volume (ml)	Total blood volume (ml)	Body haematocrit (ml/l)	Venous haematocrit (ml/l)	Haematocrit (calculated) (g/l blood)
pregnant women	2600	1400	4000	350	398	131
1st women (weeks)	3150	1450	4600	315	358	118
.....	3750	1550	5200	278	340	112
.....	3830	1600	5430	295	335	111
.....	3600	1650	5250	315	358	118

De and LAYTON, *The Physiology of Human Pregnancy*, Blackwell, Oxford, 1964, page 24

weight of the embryo and foetus¹

Embryonic age	Crown to rump length (mm)	Crown to heel length (mm)	External diameter of chorionic sac (mm)	Weight (g)	Foetal age	Crown to rump length (mm)	Crown to heel length (mm)	External diameter of abdomen (mm)
4k	0.1*	-	0.2	-	12 weeks	56.0	73.0	-
4k	0.2*	-	3	-	16 weeks	112.0	157.0	-
4k	2.0	-	10	-	20 weeks	160.0	230.0	-
4k	5.0	-	23	0.02	24 weeks	203.0	296.0	-
4k	8.0	-	25	-	28 weeks	242.0	355.0	-
4k	12.0	-	30	-	32 weeks	277.0	400.0	-
4k	17.0	17.0	40	-	36 weeks	313.0	452.0	-
4k	23.0	30.0	50	1	Full term (38 weeks)	350.0	500.0	-

length of the embryo and foetus, J. B. Developmental Anatomy, 2nd ed., Saunders, Philadelphia, 1965, page 74

Normal Body Measurements During Growth

Intrauterine growth*

Number	80 %					Weeks of pregnancy	Number	80 %				
	50 %							50 %				
	P_{10}	P_{25}	P_{50}	P_{75}	P_{90}			P_{10}	P_{25}	P_{50}	P_{75}	P_{90}
Males: Weight (kg) ¹							Females: Weight (kg) ¹					
13	0.610	0.730	0.830	1.020	1.230	24	11	0.490	0.645	0.760	0.980	1.250
12	0.685	0.790	0.880	1.040	1.260	25	15	0.600	0.740	0.845	1.050	1.295
43	0.760	0.875	0.965	1.110	1.330	26	25	0.700	0.830	0.935	1.125	1.350
38	0.835	0.970	1.080	1.215	1.435	27	34	0.790	0.925	1.035	1.210	1.420
64	0.915	1.075	1.205	1.350	1.570	28	54	0.870	1.020	1.140	1.320	1.530
80	0.995	1.180	1.330	1.495	1.720	29	63	0.945	1.115	1.255	1.455	1.690
61	1.085	1.290	1.465	1.650	1.875	30	48	1.025	1.215	1.380	1.600	1.880
88	1.195	1.415	1.600	1.830	2.050	31	59	1.125	1.330	1.515	1.760	2.100
66	1.320	1.550	1.760	2.045	2.280	32	58	1.250	1.465	1.675	1.970	2.330
62	1.470	1.710	1.970	2.310	2.575	33	56	1.400	1.630	1.875	2.275	2.620
74	1.645	1.920	2.220	2.620	2.920	34	71	1.550	1.825	2.155	2.555	2.920
104	1.875	2.180	2.520	2.885	3.190	35	84	1.730	2.060	2.410	2.795	3.160
118	2.105	2.410	2.745	3.090	3.385	36	84	1.960	2.320	2.630	2.980	3.335
188	2.330	2.625	2.930	3.245	3.540	37	184	2.220	2.520	2.800	3.120	3.450
354	2.505	2.795	3.080	3.380	3.665	38	282	2.405	2.680	2.940	3.235	3.545
504	2.630	2.915	3.200	3.505	3.780	39	506	2.540	2.810	3.060	3.340	3.640
576	2.700	2.995	3.290	3.610	3.880	40	588	2.630	2.905	3.160	3.440	3.720
312	2.735	3.035	3.330	3.670	3.940	41	320	2.660	2.950	3.210	3.520	3.795
164	2.730	3.005	3.310	3.660	3.995	42	172	2.630	2.940	3.210	3.550	3.840
Males and females: Length (cm) ²							Males and females: Head circumference (cm) ²					
30	30.8	32.9	35.5	37.5	39.9	26	24	22.4	23.6	25.2	26.6	28.5
21	31.8	34.1	36.6	38.6	41.0	27	20	23.2	24.4	25.8	27.2	28.9
46	33.0	35.5	37.8	39.8	42.2	28	40	24.3	25.4	26.7	28.0	29.4
53	34.4	36.8	39.0	40.9	43.1	29	49	25.3	26.4	27.6	28.8	30.2
47	36.1	38.3	40.3	42.2	44.5	30	49	26.2	27.4	28.6	29.7	31.1
54	37.5	39.7	41.6	43.5	45.9	31	53	26.9	28.2	29.6	30.5	31.9
62	38.8	41.1	43.2	45.0	47.2	32	58	27.6	29.0	30.4	31.4	32.7
69	39.9	42.3	44.7	46.2	48.4	33	65	28.4	29.8	31.2	32.1	33.4
111	41.0	43.4	45.8	47.3	49.4	34	103	29.2	30.6	31.9	32.9	34.0
149	42.0	44.6	46.7	48.1	50.2	35	149	30.0	31.3	32.5	33.4	34.5
189	43.1	45.6	47.4	48.8	50.9	36	186	30.6	31.8	32.9	33.8	34.9
345	44.1	46.5	48.0	49.3	51.3	37	353	31.1	32.3	33.2	34.1	35.2
595	44.9	47.1	48.4	49.8	51.7	38	611	31.4	32.5	33.4	34.3	35.4
957	45.5	47.6	48.8	50.1	52.0	39	961	31.6	32.8	33.7	34.6	35.7
1084	45.8	47.9	49.2	50.5	52.3	40	1097	31.8	33.0	34.0	34.8	35.9
589	46.0	48.1	49.5	50.8	52.6	41	587	32.0	33.2	34.2	35.0	36.0
315	46.2	48.2	49.7	51.0	52.8	42	315	32.1	33.4	34.3	35.1	36.2

* Live births in the Colorado General Hospital, Denver, between 1948 and 1961 (P = percentile).

¹ LUBCHENCO et al., *Pediatrics*, 32, 793 (1963).

² LUBCHENCO et al., *Pediatrics*, 37, 403 (1966).

Weight loss during the first days of life¹

	Average weight at birth (g)	Weight loss as per cent of birth weight					
		3rd day		5th day		7th day	
		Mean	s	Mean	s	Mean	s
Normal birth	3465	7.22	2.52	7.29	3.14	5.72	3.20
Caesarean section with labour pains ..	3580	7.19	2.09	7.65	2.83	6.06	3.31
Caesarean section without labour pains	3550	7.27	2.33	7.97	2.17	7.66	3.34

¹ Births in the Helsinki Women's Hospital between 1947 and 1952; from FURUHJELM, U., *Etud. néo-natal.*, 3, 93 (1954).

Mean weekly weight gains (in ounces and grammes) of infants with low birth weight¹

Age in months	Boys					Girls				
	Birth weight				Full term	Birth weight				Full term
	2- < 3 lb 0.91- < 1.36 kg	3- < 4 lb 1.36- < 1.81 kg	4- < 5 lb 1.81- < 2.27 kg	5- < 6 lb 2.27- < 2.72 kg		2- < 3 lb 0.91- < 1.36 kg	3- < 4 lb 1.36- < 1.81 kg	4- < 5 lb 1.81- < 2.27 kg	5- < 6 lb 2.27- < 2.72 kg	
0-1	4.0 113	4.9 139	5.6 159	5.8 164	-	4.0 113	4.9 139	5.6 159	5.1 145	-
1-3	7.2 204	7.8 221	8.3 235	8.5 241	8.3 235	6.6 187	6.9 196	6.8 193	7.0 198	7.1 201
3-6	8.1 230	7.5 213	6.7 190	6.1 173	5.3 150	7.1 201	6.6 187	6.3 179	6.1 173	5.1 145
6-9	5.1 145	4.7 133	4.4 125	4.0 113	3.7 105	5.5 156	5.1 145	5.0 142	4.6 130	3.6 102
9-12	3.5 99	3.2 91	3.0 85	2.9 82	2.5 71	3.7 105	3.2 91	2.8 79	2.4 68	2.4 68

¹ LEVIN et al., *Weight Gain, Serum Protein Levels and Health of Breast Fed and Artificially Fed Infants*, Medical Research Council, Special Report Series, No. 296, HMSO, London, 1959, pages 102 and 104.

Normal Measurements During Growth - Birth to 6 Months'

693

Weight in pounds and kilograms; other measurements in inches and centimeters (P = percentile)

Boys								Number	Girls							
90%							90%									
80%							80%									
50%							50%									
P ₉₅	P ₉₀	P ₈₅	P ₈₀	P ₇₅	P ₇₀	P ₆₅	P ₆₀		P ₉₅	P ₉₀	P ₈₅	P ₈₀	P ₇₅	P ₇₀	P ₆₅	P ₆₀
At birth									At birth							
57	62	68	7.5	8.2	8.6	8.8		121	5.8	6.0	6.5	7.1	7.8	8.7	9.0	
2.60	2.80	3.10	3.40	3.70	3.90	4.01			2.64	2.70	2.95	3.20	3.53	3.96	4.06	
18.5	19.3	19.3	19.9	20.5	20.7	20.9		118	18.5	18.5	19.2	19.5	20.1	20.5	20.9	
47.0	49.0	49.0	50.5	52.0	52.5	53.0			47.0	47.0	48.7	49.5	51.0	52.0	53.0	
1 month									1 month							
7.5	7.9	8.2	8.9	9.5	10.1	10.4		48	7.4	7.6	8.0	8.5	9.0	9.7	9.9	
5.42	5.57	5.72	6.04	6.29	6.58	6.73			3.36	3.44	3.63	3.86	4.08	4.42	4.50	
20.5	20.7	20.9	21.5	22.0	22.4	22.4		49	20.0	20.2	20.7	20.9	21.5	21.9	22.3	
52.0	52.5	53.2	54.5	55.8	56.8	57.0			50.7	51.4	52.5	53.2	54.5	55.5	56.7	
13.3	13.4	13.8	14.2	14.4	14.6	14.8		42	13.0	13.2	13.5	13.8	14.2	14.5	14.9	
33.7	34.0	35.0	36.0	36.5	37.0	37.7			33.0	33.5	34.2	35.0	36.0	36.9	37.9	
13.9	14.2	14.4	14.8	15.0	15.4	15.4		44	13.5	13.9	14.2	14.4	14.6	15.0	15.1	
35.5	36.0	36.5	37.5	38.0	39.0	39.0			34.2	35.3	36.0	36.5	37.0	38.1	38.4	
2 months									2 months							
9.4	9.8	10.4	11.0	11.8	12.4	12.5		57	9.0	9.2	9.9	10.5	11.1	11.7	12.1	
4.27	4.43	4.73	4.98	5.34	5.64	5.69			4.07	4.19	4.48	4.75	5.02	5.31	5.39	
21.9	22.0	22.4	22.8	23.2	23.4	23.8		56	21.2	21.5	22.0	22.2	22.6	23.0	23.4	
55.5	56.0	57.0	58.0	59.0	59.5	60.4			53.9	54.5	56.0	56.5	57.5	58.5	59.5	
14.0	14.4	14.6	15.0	15.4	15.6	15.7		50	13.9	14.0	14.4	14.8	15.0	15.2	15.4	
35.5	36.5	37.0	38.0	39.0	39.5	40.0			35.2	35.5	36.5	37.5	38.0	38.5	39.0	
14.8	15.0	15.2	15.4	15.7	15.9	16.0		53	14.3	14.6	14.8	15.2	15.4	15.6	15.7	
37.5	38.0	38.5	39.0	40.0	40.5	40.7			36.3	37.0	37.5	38.5	39.0	39.5	40.0	
3 months									3 months							
11.4	11.9	12.6	13.2	13.9	14.7	15.2		60	10.6	10.8	11.5	12.2	13.1	13.7	14.2	
5.18	5.40	5.73	6.00	6.32	6.66	6.90			4.80	4.89	5.20	5.53	5.95	6.23	6.46	
23.0	23.2	23.8	24.0	24.6	24.9	25.0		58	22.6	22.8	23.0	23.4	23.8	24.3	24.8	
53.3	59.0	60.5	61.0	62.5	63.2	63.6			57.4	58.0	58.5	59.5	60.5	61.6	63.0	
15.0	15.2	15.6	15.9	16.1	16.3	16.5		55	14.8	14.8	15.2	15.4	15.7	15.9	16.2	
38.0	38.5	39.5	40.5	41.0	41.5	42.0			37.5	37.5	38.5	39.0	40.0	40.5	41.2	
15.4	15.6	15.7	15.9	16.3	16.5	16.7		55	15.0	15.0	15.4	15.7	15.9	16.1	16.2	
39.0	39.5	40.0	40.5	41.5	42.0	42.5			38.0	38.2	39.0	40.0	40.5	41.0	41.2	
15.0	15.2	15.6	16.1	16.2	16.5	16.5		16	14.7	15.0	15.2	15.7	15.9	16.1	16.2	
38.0	38.6	39.7	41.0	41.2	42.0	42.0			57.4	38.0	38.5	40.0	40.5	41.0	41.2	
4 months									4 months							
12.8	13.0	14.0	15.1	15.9	16.5	17.1		58	11.5	11.9	12.7	13.8	15.1	15.7	16.4	
5.82	5.91	6.35	6.84	7.23	7.49	7.77			5.22	5.42	5.77	6.24	6.85	7.13	7.43	
23.7	24.1	25.0	25.4	25.8	26.1	26.4		58	23.4	23.6	23.8	24.4	25.0	25.4	25.4	
60.1	61.3	63.5	64.5	65.5	66.3	67.0			59.5	60.0	60.5	62.0	63.5	64.5	64.6	
15.6	15.7	16.1	16.5	16.9	17.1	17.3		56	15.0	15.4	15.7	15.9	16.3	16.5	16.6	
19.5	40.0	41.0	42.0	43.0	43.5	44.0			35.0	39.0	40.0	40.5	41.5	42.0	42.1	
15.7	15.9	16.1	16.3	16.7	16.9	17.1		55	15.4	15.4	15.7	16.1	16.4	16.7	16.9	
40.0	40.5	41.0	41.5	42.5	43.0	43.5			39.0	39.2	40.0	41.0	41.6	42.5	43.0	
5 months									5 months							
13.6	14.4	15.2	16.2	17.4	17.7	18.3		62	13.2	13.3	14.3	15.4	16.3	17.0	17.3	
6.19	6.52	6.91	7.37	7.90	8.44	8.29			6.00	6.05	6.50	7.00	7.40	7.71	7.86	
24.6	25.0	25.8	26.2	26.6	27.1	27.2		61	24.4	24.6	25.0	25.2	25.8	26.2	26.4	
62.5	63.5	65.8	66.5	67.5	68.9	69.0			62.0	62.5	63.5	64.0	65.5	66.5	67.0	
16.1	16.3	16.6	17.1	17.3	17.6	17.7		59	15.9	15.9	16.1	16.5	16.7	17.1	17.3	
40.9	41.5	42.2	43.5	44.0	44.6	45.0			40.5	40.5	41.0	42.0	42.5	43.5	44.0	
16.1	16.1	16.5	16.9	17.1	17.3	17.5		59	15.7	15.9	16.1	16.5	16.7	16.9	17.3	
41.0	41.0	42.0	43.0	43.5	44.0	44.5			40.0	40.5	41.0	42.0	42.5	43.0	44.0	
6 months									6 months							
14.9	15.4	16.5	17.9	18.7	19.3	19.8		74	14.0	14.4	15.3	16.5	17.5	18.2	19.0	
6.54	7.00	7.43	8.12	8.49	8.77	8.98			6.34	6.53	6.92	7.48	7.93	8.27	8.62	
25.2	25.6	26.4	27.0	27.4	28.1	28.2		74	25.0	25.2	25.6	26.2	26.6	27.3	27.4	
64.1	65.1	67.1	68.5	69.5	71.3	71.6			63.5	64.0	65.0	65.5	67.5	69.3	69.6	
16.5	16.7	17.1	17.5	17.7	18.1	18.3		73	16.1	16.3	16.7	16.9	17.3	17.6	17.7	
41.8	42.5	43.5	44.5	45.0	45.0	45.5			41.0	41.5	42.5	43.0	44.0	44.7	45.0	
16.5	16.7	16.9	17.1	17.5	17.7	17.9		73	16.1	16.3	16.5	16.9	17.3	17.3	17.5	
46.8	47.5	48.0	48.5	49.5	49.5	49.5			40.8	41.5	42.0	43.0	43.5	44.0	44.5	
16.5	16.7	16.9	17.3	17.7	18.1	18.1		23	15.5	16.1	16.5	16.9	17.3	17.6	17.7	
42.0	42.4	43.0	44.0	45.0	45.0	45.0			39.5	41.0	41.8	43.0	44.0	44.7	45.0	

HILFENSCHEID, J. *Birth and Age, 19, 406* (1964). From measurements made in the period 1957-1962 in northwest Switzerland on 341 boys and 325 girls, mostly of German-Swiss descent.

Normal Measurements During Growth - 7 Months to 12 Months¹Weight in pounds and kilograms; other measurements in inches and centimetres (*P* = percentile)

Boys								Girls								
Number	90%							Number	90%							
	80%						80%									
	50%					50%										
	<i>P</i> ₉₀	<i>P</i> ₈₀	<i>P</i> ₇₅	<i>P</i> ₇₀	<i>P</i> ₆₅	<i>P</i> ₆₀	<i>P</i> ₉₀		<i>P</i> ₈₀	<i>P</i> ₇₅	<i>P</i> ₇₀	<i>P</i> ₆₅	<i>P</i> ₆₀			
7 months																
50	15.9	16.3	17.3	18.4	19.5	19.9	20.2	Weight	47	14.8	15.1	16.0	17.4	18.3	19.5	20.1
	7.19	7.41	7.86	8.36	8.85	9.02	9.15			6.72	6.87	7.28	7.87	8.31	8.86	9.13
49	25.7	26.2	27.0	27.6	28.0	28.3	28.8	Length	47	25.6	25.8	26.2	26.8	27.4	27.8	28.0
	65.2	66.5	68.7	70.0	71.0	72.0	73.2			65.1	65.5	66.5	68.0	69.5	70.5	71.0
48	16.9	17.1	17.5	17.7	18.1	18.5	18.6	Sitting height	46	16.6	16.9	17.1	17.3	17.7	18.0	18.4
	43.0	43.5	44.5	45.0	46.0	47.0	47.3			42.1	42.8	43.5	44.0	45.0	45.7	46.8
48	16.7	16.9	17.1	17.3	17.7	18.0	18.1	Head circ.	46	16.3	16.5	16.9	17.1	17.5	17.7	17.8
	42.5	42.9	43.5	44.0	45.0	45.6	46.0			41.5	42.0	43.0	43.5	44.5	45.0	45.3
20	16.5	16.7	16.9	17.3	17.7	18.1	18.1	Chest circ.	16	15.7	16.1	16.7	17.3	17.7	17.7	17.8
	42.0	42.5	43.0	44.0	45.0	46.0	46.0			39.8	41.0	42.5	44.0	45.0	45.0	45.2
8 months																
59	16.8	17.8	18.4	19.8	20.7	21.3	21.8	Weight	56	15.7	15.8	16.7	18.2	19.4	20.5	21.5
	7.63	8.06	8.35	8.97	9.37	9.66	9.88			7.10	7.16	7.56	8.24	8.78	9.30	9.74
59	26.3	26.8	27.8	28.1	28.6	29.1	29.3	Length	55	26.2	26.4	26.8	27.4	28.0	28.4	28.7
	66.9	68.0	70.5	71.5	72.6	74.0	74.5			66.5	67.0	68.0	69.5	71.0	72.2	73.0
57	17.1	17.3	17.7	18.1	18.5	18.7	18.9	Sitting height	55	16.9	17.1	17.5	17.7	18.1	18.4	18.5
	43.4	44.0	45.0	46.0	47.0	47.5	48.0			42.8	43.5	44.5	45.0	46.0	46.7	47.0
56	16.9	16.9	17.5	17.7	18.1	18.3	18.3	Head circ.	55	16.5	16.8	17.1	17.5	17.7	18.1	18.1
	43.0	43.0	44.5	45.0	46.0	46.5	46.5			42.0	42.7	43.5	44.5	45.0	46.0	46.0
19	16.9	16.9	17.3	17.7	18.1	18.3	18.5	Chest circ.	20	16.7	16.7	16.9	17.7	18.1	18.5	18.7
	42.8	43.0	44.0	45.0	46.0	46.5	46.9			42.5	42.5	43.0	45.0	46.0	47.0	47.5
9 months																
66	17.6	18.3	19.2	20.7	21.6	22.8	22.9	Weight	72	16.1	16.8	17.4	18.9	20.3	21.4	21.8
	8.00	8.30	8.71	9.37	9.82	10.36	10.40			7.30	7.62	7.90	8.58	9.23	9.71	9.88
66	27.1	28.0	28.3	28.7	29.1	29.5	29.8	Length	72	26.7	27.0	27.4	28.0	28.3	28.9	29.1
	68.8	71.0	72.0	73.0	74.0	75.0	75.8			67.9	68.6	69.5	71.0	72.0	73.5	74.0
63	17.5	17.7	18.1	18.3	18.7	19.0	19.3	Sitting height	72	17.0	17.3	17.7	17.9	18.3	18.5	18.8
	44.5	45.0	46.0	46.5	47.5	48.3	49.0			43.3	44.0	45.0	45.5	46.5	47.0	47.7
65	17.3	17.3	17.7	18.1	18.3	18.5	18.7	Head circ.	72	16.9	16.9	17.3	17.7	17.9	18.1	18.3
	44.0	44.0	45.0	46.0	46.5	47.0	47.5			42.8	43.0	44.0	45.0	45.5	46.0	46.5
24	17.2	17.3	17.3	17.9	18.5	18.5	18.8	Chest circ.	26	16.7	16.9	17.3	17.7	18.2	18.6	18.8
	43.6	44.0	44.0	45.5	47.0	47.0	47.8			42.5	43.0	44.0	45.0	46.2	47.2	47.8
10 months																
36	17.6	18.3	19.5	20.7	21.6	22.9	23.5	Weight	36	16.8	17.3	18.3	19.3	20.4	21.8	22.2
	8.00	8.30	8.85	9.40	9.82	10.41	10.66			7.60	7.84	8.30	8.74	9.25	9.90	10.07
36	27.5	28.0	28.5	28.9	29.3	30.1	30.4	Length	36	27.0	27.2	27.8	28.3	28.7	29.1	29.4
	69.9	71.0	72.5	73.5	74.5	76.4	77.1			68.5	69.1	70.5	72.0	73.0	74.0	74.7
34	17.7	17.7	18.1	18.3	18.7	19.1	19.3	Sitting height	36	17.2	17.4	17.7	18.1	18.5	18.6	18.9
	45.0	45.0	46.0	46.5	47.5	48.5	49.0			43.8	44.3	45.0	46.0	47.0	47.2	48.0
36	17.3	17.3	17.7	18.1	18.5	18.5	18.8	Head circ.	34	16.9	16.9	17.3	17.7	18.0	18.1	18.3
	44.0	44.0	45.0	46.0	47.0	47.0	47.8			43.0	43.0	44.0	45.0	45.7	46.0	46.5
11 months																
28	18.7	19.5	20.7	22.0	23.1	23.5	23.9	Weight	34	17.1	17.6	18.6	20.2	22.0	23.3	24.0
	8.50	8.86	9.37	10.00	10.46	10.64	10.86			7.77	8.00	8.43	9.14	9.99	10.59	10.90
28	28.1	28.9	29.1	29.7	29.9	30.4	30.6	Length	34	27.8	27.9	28.1	28.9	29.4	29.7	30.2
	71.3	73.3	74.0	75.5	76.0	77.1	77.8			70.5	70.8	71.5	73.5	74.7	75.5	76.6
28	17.9	18.1	18.3	18.7	18.9	19.3	19.5	Sitting height	33	17.4	17.6	18.0	18.4	18.7	19.0	19.2
	45.4	46.0	46.5	47.5	48.0	49.0	49.6			44.3	44.6	45.6	46.7	47.5	48.3	48.8
27	17.5	17.7	17.9	18.5	18.7	18.9	18.9	Head circ.	33	17.2	17.3	17.5	17.9	18.1	18.5	18.5
	44.5	45.0	45.5	47.0	47.5	48.0	48.0			43.8	44.0	44.5	45.5	46.0	46.9	47.1
12 months																
58	18.7	20.2	21.1	22.2	23.8	24.5	25.0	Weight	73	18.1	18.5	19.5	21.0	22.1	24.4	25.0
	8.50	9.17	9.57	10.09	10.78	11.13	11.36			8.22	8.40	8.86	9.51	10.04	11.05	11.33
58	28.1	28.9	29.5	30.1	30.5	31.1	31.3	Length	72	28.0	28.3	28.7	29.4	29.9	30.3	30.5
	71.4	73.4	75.0	76.5	77.5	79.0	79.5			71.0	72.0	73.0	74.7	76.0	77.0	77.5
56	18.0	18.3	18.7	18.9	19.3	20.0	20.1	Sitting height	71	17.5	17.7	18.2	18.7	18.9	19.3	19.5
	45.8	46.5	47.5	48.0	49.0	50.7	51.1			44.5	45.0	46.3	47.5	48.0	48.9	49.5
58	17.5	17.7	18.1	18.5	18.9	19.1	19.1	Head circ.	72	17.2	17.5	17.7	18.1	18.3	18.5	18.7
	44.5	45.0	46.0	47.0	48.0	48.5	48.5			43.8	44.5	45.0	46.0	46.5	47.0	47.5
26	17.5	17.6	18.1	18.5	18.9	19.3	19.6	Chest circ.	31	16.7	17.3	17.8	18.1	18.5	18.7	19.0
	44.5	44.8	46.0	47.0	48.0	49.0	49.7			42.5	44.0	45.3	46.0	47.1	47.5	48.2

¹ HEIMENDINGER, J., *Helv. paediat. Acta*, 19, 406 (1964). From measurements made in the period 1957-1962 in northwest Switzerland on 341 boys and 326 girls mostly of German-Swiss descent.

Normal Measurements During Growth - 15 Months to 2 Years

695

Weight in pounds and kilogrammes, other measurements in inches and centimetres (P = percentile)

Boys								Number	Girls							
90%									90%							
80%									80%							
50%									50%							
P ₉₀	P ₈₀	P ₇₀	P ₆₀	P ₅₀	P ₄₀	P ₃₀	P ₂₀		P ₉₀	P ₈₀	P ₇₀	P ₆₀	P ₅₀	P ₄₀	P ₃₀	P ₂₀
15 months ¹								15 months ¹								
20.8	21.6	22.5	24.0	25.3	26.9	28.5		46	19.7	20.0	21.4	22.4	24.1	24.9	25.6	
9.45									8.92	9.06	9.69	10.15	10.92	11.29	11.61	
29.6								46	29.5	29.7	30.1	30.7	31.3	31.7	31.9	
75.2									75.0	75.5	76.5	78.0	79.5	80.5	81.0	
18.8								46	18.3	18.3	18.9	19.1	19.5	20.0	20.2	
47.8									46.5	46.5	48.0	48.5	49.5	50.7	51.3	
17.9								45	17.5	17.7	18.1	18.5	18.7	18.9	19.1	
45.5									44.5	45.0	46.0	47.0	47.5	48.0	48.5	
17.9								28	17.1	17.6	18.1	18.5	18.7	18.9	19.4	
45.5									43.4	44.8	46.0	47.0	47.5	48.1	49.4	
18 months ¹								18 months ¹								
22.3	22.8	24.1	24.9	26.5	28.5	29.3		40	21.1	22.4	23.1	24.1	26.2	27.4	28.7	
								40	3							
								40	7							
								40	1							
								40	4							
								22	1							
									4							
2 years ¹								2 years ¹								
24.1	25.0	26.1	27.6	29.5	30.7	31.8		24	22.1	23.3	24.7	26.7	28.6	30.7	31.0	
10.91								24								
33.1								24								
84.0																
20.1								24								
51.1																
18.5								24								
47.1																
18.7								10								
47.5																
95%								95%								
80%								80%								
50%								50%								
P ₉₀	P ₈₀	P ₇₀	P ₆₀	P ₅₀	P ₄₀	P ₃₀	P ₂₀	P ₉₀	P ₈₀	P ₇₀	P ₆₀	P ₅₀	P ₄₀	P ₃₀	P ₂₀	P ₁₀
2 years ²								2 years ²								
8.3	21.4	24.3	27.3	30.4	33.3	36.4	4.5	20.1	22.3	24.0	26.2	28.4	30.2	32.4	3.1	
8.3	9.7	11.0	12.4	13.8	15.1	16.5	2.03	9.1	10.1	10.9	11.9	12.9	13.7	14.7	1.4	
31.1	32.2	33.1	34.3	35.4	36.3	37.4	1.6	31.0	32.0	33.0	34.1	35.1	36.1	37.1	1.5	
79.9	81.7	84.2	87.0	89.8	92.3	95.1	4.1	78.8	81.4	83.8	86.5	89.2	91.6	94.2	3.9	
18.9	19.6	20.2	20.8	21.5	22.0	22.7	0.9	18.3	19.1	19.9	20.7	21.6	22.4	23.2	1.3	
44.1	49.3	51.3	52.9	54.5	56.0	57.7	2.4	46.4	48.6	50.5	52.7	54.9	56.8	59.0	3.2	
4.9	5.8	6.7	7.6	8.5	9.4	10.3	1.4	5.9	6.6	7.2	7.9	8.5	9.1	9.8	1.0	
12.4	14.8	16.9	19.3	21.7	23.8	26.2	3.5	15.0	16.8	18.3	20.0	21.7	23.2	25.0	2.5	
4.6	5.4	6.1	6.9	7.7	8.5	9.3	1.2	4.9	5.5	6.0	6.6	7.2	7.7	8.4	0.9	
11.7	13.7	15.6	17.6	19.6	21.5	23.5	3.0	12.4	14.0	15.3	16.8	18.3	19.6	21.2	2.2	
18.3	18.7	19.0	19.4	19.8	20.1	20.5	0.6	17.6	18.0	18.3	18.7	19.1	19.4	19.8	0.6	
45.4	47.4	48.2	49.2	50.2	51.0	52.0	1.4	44.6	45.6	46.4	47.4	48.4	49.2	50.2	1.4	
17.8	18.4	18.9	19.5	20.1	20.6	21.3	0.9	17.1	17.8	18.4	19.0	19.6	20.2	20.9	0.9	
45.2	46.8	48.1	49.6	51.1	52.4	54.0	2.2	43.5	45.2	46.7	48.3	49.9	51.4	53.1	2.4	
5.3	5.6	5.8	6.1	6.4	6.6	6.9	0.4	4.1	4.7	5.2	5.8	6.3	6.9	7.4	0.8	
13.5	14.2	14.8	15.5	16.2	16.8	17.5	1.0	10.5	12.0	13.3	14.7	16.1	17.4	18.9	2.1	
1.6	2.4	3.1	3.9	4.7	5.5	6.3	1.2	1.6	2.4	3.0	3.8	4.5	5.2	5.9	1.1	
4.1	6.1	8.0	10.0	12.0	13.9	15.9	3.0	4.1	6.0	7.7	9.6	11.5	13.2	15.1	2.8	
6.7	7.0	7.2	7.5	7.8	8.0	8.3	0.4	5.6	6.2	6.7	7.3	7.9	8.4	9.0	0.9	
17.0	17.7	18.3	19.0	19.7	20.3	21.0	1.0	14.1	15.7	17.0	18.5	20.0	21.3	22.9	2.2	

¹ HERSHBERGER, J., *Helv. paediat. Acta*, 19, 406 (1964). From measurements made in the period 1957-1962 in north-east Switzerland on 341 boys and 256 girls mostly of German-Swiss descent.

² HERSHBERGER, J., *Helv. paediat. Acta*, 19, suppl. 13 (1964). From measurements made in the period 1956-1957 on 2150 boys and 2150 girls in Basle, Switzerland.

Normal Measurements During Growth - 2½ Years to 3½ Years¹ Weight in pounds and kilograms; other measurements in inches and centimetres (P = percentile)

Boys								Girls								
95%								95%								
80%								80%								
50%								50%								
P _{2.5}	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P _{97.5}	s	P _{2.5}	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P _{97.5}	s	
2½ years																
20.5	23.8	26.7	29.8	32.8	35.7	39.0	4.7	Weight	21.4	24.0	26.2	28.9	31.5	33.7	36.4	3.7
9.3	10.8	12.1	13.5	14.9	16.2	17.7	2.11	Height	9.7	10.9	11.9	13.1	14.3	15.3	16.5	1.7
33.1	34.3	35.2	36.4	37.5	38.5	39.6	1.7	Sitting height	32.6	33.7	34.7	35.8	36.9	37.9	39.0	1.6
84.1	87.0	89.5	92.4	95.3	97.8	100.7	4.2	Shoulder width	82.9	85.7	88.2	91.0	93.8	96.3	99.1	4.1
19.6	20.3	20.9	21.6	22.3	23.0	23.6	1.0	Pelvic width	18.8	19.6	20.4	21.2	22.0	22.8	23.6	1.2
49.8	51.5	53.1	54.9	56.7	58.3	60.0	2.6	Head circ.	47.7	49.8	51.7	53.8	55.9	57.8	59.9	3.1
5.2	6.1	7.0	8.0	8.9	9.8	10.7	1.4	Chest circ.	6.2	6.9	7.5	8.1	8.8	9.4	10.1	1.0
13.1	15.5	17.7	20.2	22.7	24.9	27.3	3.6	Upper arm circ.	15.7	17.5	19.0	20.7	22.4	23.9	25.7	2.5
4.5	5.4	6.1	7.0	7.9	8.6	9.5	1.3	Wrist circ.	5.0	5.6	6.2	6.8	7.4	8.0	8.6	0.9
11.5	13.7	15.6	17.8	20.0	21.9	24.1	3.2	Calf circ.	12.7	14.3	15.7	17.3	18.9	20.3	21.9	2.3
18.4	18.8	19.1	19.5	19.9	20.2	20.6	0.6	Weight	17.8	18.2	18.5	18.9	19.3	19.6	20.0	0.6
46.8	47.8	48.6	49.6	50.6	51.4	52.4	1.4	Height	45.3	46.3	47.1	48.1	49.1	49.9	50.9	1.4
17.9	18.5	19.1	19.8	20.4	21.0	21.7	0.9	Sitting height	17.5	18.2	18.8	19.4	20.0	20.6	21.3	0.9
45.4	47.1	48.6	50.2	51.8	53.3	55.0	2.4	Shoulder width	44.5	46.2	47.7	49.3	50.9	52.4	54.1	2.4
5.2	5.5	5.8	6.1	6.5	6.8	7.1	0.5	Pelvic width	4.3	4.9	5.4	5.9	6.5	6.9	7.5	0.8
13.2	14.0	14.8	15.6	16.4	17.2	18.0	1.2	Head circ.	11.0	12.4	13.6	15.0	16.4	17.6	19.0	2.0
1.7	2.5	3.2	4.0	4.8	5.6	6.3	1.2	Chest circ.	1.5	2.3	3.0	3.8	4.6	5.3	6.0	1.1
4.3	6.3	8.2	10.2	12.2	14.1	16.1	3.0	Upper arm circ.	3.9	5.8	7.6	9.6	11.6	13.4	15.3	2.9
6.1	6.7	7.1	7.7	8.2	8.7	9.3	0.8	Wrist circ.	5.8	6.4	6.9	7.5	8.1	8.6	9.3	0.9
15.5	16.9	18.1	19.5	20.9	22.1	23.5	2.0	Calf circ.	14.7	16.3	17.6	19.1	20.6	21.9	23.5	2.2
3 years																
23.1	26.2	29.1	32.2	35.3	38.1	41.2	4.5	Weight	22.7	25.8	28.4	31.5	34.6	37.3	40.3	4.4
10.5	11.9	13.2	14.6	16.0	17.3	18.7	2.06	Height	10.3	11.7	12.9	14.3	15.7	16.9	18.3	2.0
34.7	35.8	36.8	37.9	39.0	40.0	41.1	1.6	Sitting height	34.1	35.3	36.3	37.5	38.6	39.7	40.8	1.7
88.2	91.0	93.5	96.3	99.1	101.6	104.4	4.1	Shoulder width	86.7	89.6	92.3	95.2	98.1	100.8	103.7	4.3
19.7	20.5	21.3	22.1	22.9	23.7	24.5	1.2	Pelvic width	19.4	20.1	20.8	21.6	22.4	23.1	23.9	1.1
50.0	52.1	54.0	56.1	58.2	60.1	62.2	3.1	Head circ.	49.2	51.1	52.9	54.9	56.9	58.7	60.6	2.9
5.4	6.4	7.3	8.3	9.3	10.2	11.2	1.5	Chest circ.	6.4	7.0	7.7	8.4	9.1	9.7	10.4	1.0
13.8	16.3	18.6	21.1	23.6	25.9	28.4	3.7	Upper arm circ.	16.2	17.9	19.5	21.3	23.1	24.7	26.4	2.6
4.4	5.4	6.2	7.1	8.1	8.9	9.8	1.4	Wrist circ.	5.2	5.8	6.3	7.0	7.6	8.1	8.8	0.9
11.2	13.6	15.7	18.1	20.5	22.6	25.0	3.5	Calf circ.	13.1	14.7	16.1	17.7	19.3	20.7	22.3	2.3
18.5	18.9	19.3	19.6	20.0	20.4	20.7	0.6	Weight	18.0	18.4	18.7	19.1	19.5	19.9	20.3	0.6
47.1	48.1	48.9	49.9	50.9	51.7	52.7	1.4	Height	45.6	46.7	47.6	48.6	49.6	50.5	51.6	1.5
17.3	18.2	19.1	20.0	20.9	21.8	22.7	1.4	Sitting height	17.9	18.6	19.2	19.8	20.5	21.1	21.8	1.0
43.9	46.3	48.4	50.8	53.2	55.3	57.7	3.5	Shoulder width	45.4	47.2	48.7	50.4	52.1	53.6	55.4	2.5
5.1	5.5	5.8	6.2	6.6	6.9	7.3	0.6	Pelvic width	4.5	5.0	5.5	6.0	6.5	7.0	7.5	0.7
12.9	13.9	14.7	15.7	16.7	17.5	18.5	1.4	Head circ.	11.5	12.8	14.0	15.3	16.6	17.8	19.1	1.9
1.7	2.5	3.3	4.1	4.9	5.7	6.5	1.2	Chest circ.	1.5	2.3	3.1	3.9	4.6	5.4	6.2	1.2
4.3	6.4	8.3	10.4	12.5	14.4	16.5	3.1	Upper arm circ.	3.9	5.9	7.8	9.8	11.8	13.7	15.7	3.0
6.2	6.8	7.3	7.8	8.4	8.9	9.5	0.8	Wrist circ.	6.2	6.7	7.2	7.7	8.2	8.7	9.2	0.7
15.7	17.2	18.5	19.9	21.3	22.6	24.1	2.1	Calf circ.	15.8	17.1	18.3	19.6	20.9	22.1	23.4	1.9
3½ years																
25.8	28.9	31.5	34.6	37.7	40.3	43.4	4.5	Weight	24.0	27.6	30.4	33.7	37.0	39.9	43.4	4.9
11.7	13.1	14.3	15.7	17.1	18.3	19.7	2.03	Height	10.9	12.5	13.8	15.3	16.8	18.1	19.7	2.2
36.1	37.2	38.2	39.4	40.5	41.5	42.6	1.7	Sitting height	35.5	36.7	37.7	38.9	40.1	41.1	42.3	1.7
91.7	94.6	97.1	100.0	102.9	105.4	108.3	4.2	Shoulder width	90.1	93.1	95.8	98.8	101.8	104.5	107.5	4.4
19.5	20.5	21.5	22.5	23.6	24.5	25.6	1.5	Pelvic width	19.9	20.6	21.3	22.0	22.8	23.5	24.2	1.1
49.5	52.1	54.5	57.2	59.9	62.3	64.9	3.9	Head circ.	50.5	52.4	54.1	56.0	57.9	59.6	61.5	2.8
5.8	6.8	7.6	8.6	9.6	10.5	11.4	1.4	Chest circ.	6.7	7.3	8.0	8.7	9.4	10.0	10.7	1.0
14.8	17.2	19.4	21.9	24.4	26.6	29.0	3.6	Upper arm circ.	16.9	18.6	20.2	22.0	23.8	25.4	27.1	2.6
4.2	5.2	6.2	7.2	8.3	9.3	10.3	1.5	Wrist circ.	5.4	6.0	6.5	7.1	7.7	8.2	8.9	0.9
10.7	13.3	15.7	18.4	21.1	23.5	26.1	3.9	Calf circ.	13.7	15.3	16.6	18.1	19.6	20.9	22.5	2.2
18.7	19.1	19.4	19.8	20.2	20.5	20.9	0.6	Weight	18.3	18.7	19.0	19.3	19.7	20.0	20.4	0.5
47.5	48.5	49.3	50.3	51.3	52.1	53.1	1.4	Height	46.5	47.4	48.2	49.1	50.0	50.8	51.7	1.3
15.2	17.0	18.5	20.2	22.0	23.5	25.2	2.5	Sitting height	18.2	18.9	19.5	20.2	20.9	21.5	22.2	1.0
38.7	43.1	47.0	51.4	55.8	59.7	64.1	6.4	Shoulder width	46.3	48.1	49.6	51.3	53.0	54.5	56.3	2.5
4.8	5.3	5.7	6.2	6.7	7.1	7.6	0.7	Pelvic width	4.8	5.3	5.7	6.1	6.6	7.0	7.5	0.7
12.2	13.5	14.6	15.8	17.0	18.1	19.4	1.8	Head circ.	12.2	13.4	14.4	15.6	16.8	17.8	19.0	1.7
1.8	2.6	3.3	4.2	5.0	5.7	6.6	1.2	Chest circ.	1.6	2.4	3.1	3.9	4.7	5.5	6.3	1.2
4.5	6.6	8.5	10.6	12.7	14.6	16.7	3.1	Upper arm circ.	4.1	6.1	8.0	10.0	12.0	13.9	15.9	3.0
6.3	6.9	7.4	8.0	8.6	9.1	9.8	0.9	Wrist circ.	6.7	7.2	7.5	7.9	8.3	8.7	9.1	0.6
16.0	17.6	18.9	20.4	21.9	23.2	24.8	2.2	Calf circ.	17.1	18.2	19.1	20.1	21.1	22.0	23.1	1.5

¹ HEIMENDINGER, J., *Helv. paediat. Acta*, 19, suppl. 13 (1964). From measurements made in the period 1956-1957 on 2150 boys and 2150 girls in Basle, Switzerland.

Normal Measurements During Growth - 4 Years to 5 Years¹

997

Weight in pounds and kilograms, other measurements in inches and centimetres (P = percentile)

Boys										Girls									
95%										95%									
80%										80%									
50%										50%									
P ₁₀	P ₁₅	P ₂₀	P ₂₅	P ₃₀	P ₃₅	P ₄₀	P ₄₅	P ₅₀	P ₅₅	P ₆₀	P ₆₅	P ₇₀	P ₇₅	P ₈₀	P ₈₅	P ₉₀	P ₉₅	P ₁₀₀	P ₁₀₅
4 years										4 years									
Weight	25.8	29.3	32.4	35.9	39.5	42.5	46.1	5.1		Weight	25.8	29.3	32.4	35.9	39.5	42.5	46.1	5.1	
Height	11.7	13.5	14.7	16.3	17.9	19.3	20.9	2.3		Height	11.7	13.5	14.7	16.3	17.9	19.3	20.9	2.3	
Sitting height	36.8	38.0	39.1	40.3	41.5	42.6	43.8	1.8		Sitting height	36.8	38.0	39.1	40.3	41.5	42.6	43.8	1.8	
Shoulder width	93.4	96.5	99.2	102.3	105.4	108.1	111.2	4.5		Shoulder width	93.4	96.5	99.2	102.3	105.4	108.1	111.2	4.5	
Pelvic width	20.4	21.1	21.8	22.5	23.2	23.9	24.6	1.1		Pelvic width	20.4	21.1	21.8	22.5	23.2	23.9	24.6	1.1	
Head circ.	51.8	53.6	55.3	57.1	58.9	60.6	62.4	2.7		Head circ.	51.8	53.6	55.3	57.1	58.9	60.6	62.4	2.7	
Chest circ.	6.9	7.6	8.2	8.9	9.6	10.3	10.9	1.0		Chest circ.	6.9	7.6	8.2	8.9	9.6	10.3	10.9	1.0	
Upper arm circ.	17.6	19.3	20.9	22.7	24.5	26.1	27.8	2.6		Upper arm circ.	17.6	19.3	20.9	22.7	24.5	26.1	27.8	2.6	
Wrist circ.	5.6	6.2	6.7	7.3	7.8	8.3	8.7	0.8		Wrist circ.	5.6	6.2	6.7	7.3	7.8	8.3	8.7	0.8	
Calf circ.	14.5	15.8	17.1	18.5	19.9	21.2	22.2	2.1		Calf circ.	14.5	15.8	17.1	18.5	19.9	21.2	22.2	2.1	
	18.5	18.9	19.2	19.5	19.9	20.2	20.6	0.5			18.5	18.9	19.2	19.5	19.9	20.2	20.6	0.5	
	47.0	47.9	48.7	49.6	50.5	51.3	52.2	1.3			47.0	47.9	48.7	49.6	50.5	51.3	52.2	1.3	
	18.4	19.1	19.7	20.4	21.0	21.6	22.3	1.0			18.4	19.1	19.7	20.4	21.0	21.6	22.3	1.0	
	46.7	48.5	50.0	51.7	53.4	54.9	56.7	2.5			46.7	48.5	50.0	51.7	53.4	54.9	56.7	2.5	
	5.2	5.6	5.9	6.3	6.7	7.0	7.4	0.6			5.2	5.6	5.9	6.3	6.7	7.0	7.4	0.6	
	13.1	14.1	14.9	15.9	16.9	17.7	18.7	1.4			13.1	14.1	14.9	15.9	16.9	17.7	18.7	1.4	
	1.8	2.6	3.3	4.1	4.8	5.6	6.3	1.1			1.8	2.6	3.3	4.1	4.8	5.6	6.3	1.1	
	4.6	6.5	8.3	10.3	12.3	14.1	16.0	2.9			4.6	6.5	8.3	10.3	12.3	14.1	16.0	2.9	
	7.0	7.4	7.8	8.1	8.5	8.9	9.3	0.6			7.0	7.4	7.8	8.1	8.5	8.9	9.3	0.6	
	17.9	18.9	19.7	20.7	21.7	22.5	23.5	1.4			17.9	18.9	19.7	20.7	21.7	22.5	23.5	1.4	
4½ years										4½ years									
Weight	27.6	31.3	34.6	38.1	41.7	45.0	48.7	5.3		Weight	27.6	31.3	34.6	38.1	41.7	45.0	48.7	5.3	
Height	12.5	14.2	15.7	17.3	18.9	20.4	22.1	2.4		Height	12.5	14.2	15.7	17.3	18.9	20.4	22.1	2.4	
Sitting height	38.1	39.4	40.4	41.7	42.9	43.9	45.2	1.8		Sitting height	38.1	39.4	40.4	41.7	42.9	43.9	45.2	1.8	
Shoulder width	96.9	100.0	102.7	105.8	108.9	111.6	114.7	4.5		Shoulder width	96.9	100.0	102.7	105.8	108.9	111.6	114.7	4.5	
Pelvic width	20.7	21.4	22.1	22.9	23.7	24.4	25.2	1.1		Pelvic width	20.7	21.4	22.1	22.9	23.7	24.4	25.2	1.1	
Head circ.	52.5	54.4	56.2	58.2	60.2	62.0	63.9	2.9		Head circ.	52.5	54.4	56.2	58.2	60.2	62.0	63.9	2.9	
Chest circ.	7.3	8.0	8.5	9.2	9.8	10.4	11.1	0.9		Chest circ.	7.3	8.0	8.5	9.2	9.8	10.4	11.1	0.9	
Upper arm circ.	18.5	20.2	21.7	23.5	24.9	26.4	28.1	2.4		Upper arm circ.	18.5	20.2	21.7	23.5	24.9	26.4	28.1	2.4	
Wrist circ.	6.0	6.5	7.0	7.4	7.9	8.3	8.9	0.7		Wrist circ.	6.0	6.5	7.0	7.4	7.9	8.3	8.9	0.7	
Calf circ.	15.3	16.6	17.7	18.9	20.1	21.2	22.5	1.8		Calf circ.	15.3	16.6	17.7	18.9	20.1	21.2	22.5	1.8	
	18.6	19.0	19.3	19.7	20.1	20.4	20.8	0.6			18.6	19.0	19.3	19.7	20.1	20.4	20.8	0.6	
	47.2	48.2	49.0	50.0	51.0	51.8	52.8	1.4			47.2	48.2	49.0	50.0	51.0	51.8	52.8	1.4	
	18.5	19.2	19.8	20.5	21.2	21.9	22.5	1.0			18.5	19.2	19.8	20.5	21.2	21.9	22.5	1.0	
	47.0	48.7	50.5	52.1	53.9	55.5	57.2	2.6			47.0	48.7	50.5	52.1	53.9	55.5	57.2	2.6	
	5.4	5.7	6.1	6.4	6.7	7.0	7.3	0.5			5.4	5.7	6.1	6.4	6.7	7.0	7.3	0.5	
	13.8	14.6	15.4	16.2	17.0	17.8	18.6	1.2			13.8	14.6	15.4	16.2	17.0	17.8	18.6	1.2	
	2.2	2.9	3.5	4.1	4.8	5.6	6.3	1.1			2.2	2.9	3.5	4.1	4.8	5.6	6.3	1.1	
	5.5	7.3	9.0	10.8	12.6	14.3	16.1	2.7			5.5	7.3	9.0	10.8	12.6	14.3	16.1	2.7	
	7.2	7.6	8.0	8.3	8.7	9.1	9.4	0.6			7.2	7.6	8.0	8.3	8.7	9.1	9.4	0.6	
	18.4	19.4	20.2	21.2	22.2	23.0	24.0	1.4			18.4	19.4	20.2	21.2	22.2	23.0	24.0	1.4	
5 years										5 years									
Weight	29.8	33.5	36.8	40.3	43.9	47.2	50.9	5.3		Weight	29.8	33.5	36.8	40.3	43.9	47.2	50.9	5.3	
Height	13.5	15.2	16.7	18.5	19.9	21.4	23.1	2.4		Height	13.5	15.2	16.7	18.5	19.9	21.4	23.1	2.4	
Sitting height	39.6	40.7	41.8	43.0	44.2	45.2	46.4	1.7		Sitting height	39.6	40.7	41.8	43.0	44.2	45.2	46.4	1.7	
Shoulder width	101.1	104.2	107.1	110.2	113.3	116.2	119.3	4.6		Shoulder width	101.1	104.2	107.1	110.2	113.3	116.2	119.3	4.6	
Pelvic width	21.5	22.2	22.9	23.7	24.5	25.2	25.9	1.1		Pelvic width	21.5	22.2	22.9	23.7	24.5	25.2	25.9	1.1	
Head circ.	54.5	56.4	58.2	60.2	62.2	64.0	65.9	2.9		Head circ.	54.5	56.4	58.2	60.2	62.2	64.0	65.9	2.9	
Chest circ.	7.4	8.3	8.9	9.5	10.2	10.7	11.1	0.9		Chest circ.	7.4	8.3	8.9	9.5	10.2	10.7	11.1	0.9	
Upper arm circ.	18.9	21.2	22.6	24.2	25.8	27.2	28.1	2.3		Upper arm circ.	18.9	21.2	22.6	24.2	25.8	27.2	28.1	2.3	
Wrist circ.	5.0	6.6	7.1	7.7	8.3	8.8	9.4	0.9		Wrist circ.	5.0	6.6	7.1	7.7	8.3	8.8	9.4	0.9	
Calf circ.	15.1	16.7	18.0	19.5	21.0	22.3	23.9	2.2		Calf circ.	15.1	16.7	18.0	19.5	21.0	22.3	23.9	2.2	
	18.9	19.3	19.7	20.1	20.5	20.8	21.3	0.6			18.9	19.3	19.7	20.1	20.5	20.8	21.3	0.6	
	48.0	49.1	50.0	51.0	52.0	52.9	54.0	1.5			48.0	49.1	50.0	51.0	52.0	52.9	54.0	1.5	
	15.9	17.7	19.3	21.0	22.8	24.5	26.1	2.6			15.9	17.7	19.3	21.0	22.8	24.5	26.1	2.6	
	40.5	41.0	49.0	53.4	57.8	61.8	66.3	6.5			40.5	41.0	49.0	53.4	57.8	61.8	66.3	6.5	
	5.0	5.5	5.9	6.4	6.9	7.3	7.8	0.7			5.0	5.5	5.9	6.4	6.9	7.3	7.8	0.7	
	12.7	14.0	15.1	16.3	17.5	18.6	19.9	1.8			12.7	14.0	15.1	16.3	17.5	18.6	19.9	1.8	
	2.2	3.0	3.7	4.4	5.2	5.9	6.7	1.1			2.2	3.0	3.7	4.4	5.2	5.9	6.7	1.1	
	5.6	7.5	9.3	11.3	13.3	15.1	17.0	2.9			5.6	7.5	9.3	11.3	13.3	15.1	17.0	2.9	
	6.7	7.4	8.0	8.6	9.2	9.8	10.5	0.9			6.7	7.4	8.0	8.6	9.2	9.8	10.5	0.9	
	17.0	18.7	20.2	21.8	23.4	24.9	26.6	2.4			17.0	18.7	20.2	21.8	23.4	24.9	26.6	2.4	

¹ HENNINGSEN, J., *His paediatr Acta* 19, suppl 13 (1964) From measurements made in the period 1956-1957 on 2150 boys and 2150 girls in Basle, Switzerland

Boys								Girls								
95%								95%								
80%								80%								
50%								50%								
$P_{1.5}$	P_{10}	P_{25}	P_{50}	P_{75}	P_{90}	$P_{97.5}$	s		$P_{1.5}$	P_{10}	P_{25}	P_{50}	P_{75}	P_{90}	$P_{97.5}$	s
								5½ years								
34.2	37.7	40.8	44.1	47.4	50.5	54.0	5.0	Weight	31.7	35.7	39.0	42.8	46.5	49.8	53.8	5.3
15.5	17.1	18.5	20.0	21.5	22.9	24.5	2.25	Height	14.4	16.2	17.7	19.4	21.1	22.6	24.4	2.4
40.9	42.2	43.3	44.6	45.9	47.1	48.4	1.9	Sitting height	40.8	42.0	43.1	44.3	45.6	46.6	47.8	1.8
103.9	107.2	110.1	113.4	116.7	119.6	122.9	4.8	Shoulder width	103.7	106.8	109.5	112.6	115.7	118.4	121.5	4.3
21.8	22.6	23.3	24.1	24.9	25.6	26.4	1.2	Pelvic width	21.3	22.2	22.9	23.8	24.6	25.4	26.3	1.2
55.3	57.3	59.2	61.2	63.2	65.1	67.1	3.0	Head circ.	54.1	56.3	58.2	60.4	62.6	64.5	66.7	3.2
7.8	8.7	9.2	9.8	10.4	10.9	11.3	0.9	Chest circ.	8.1	8.7	9.2	9.7	10.3	10.7	11.3	0.8
19.8	22.1	23.4	24.9	26.4	27.7	28.6	2.2	Upper arm circ.	20.7	22.1	23.3	24.7	26.1	27.3	28.7	2.6
6.1	6.7	7.2	7.8	8.3	8.9	9.4	0.8	Wrist circ.	6.5	6.9	7.3	7.8	8.3	8.7	9.1	0.7
15.6	17.1	18.4	19.8	21.2	22.5	24.0	2.1	Calf circ.	16.4	17.6	18.6	19.8	21.0	22.0	23.2	1.7
18.9	19.3	19.7	20.2	20.6	21.0	21.4	0.6		18.7	19.1	19.5	19.9	20.4	20.7	21.2	0.6
48.0	49.1	50.1	51.2	52.3	53.3	54.4	1.6		47.4	48.5	49.5	50.6	51.7	52.7	53.8	1.6
18.0	19.1	20.2	21.3	22.5	23.5	24.7	1.7		18.7	19.4	20.1	20.8	21.5	22.2	22.9	1.1
45.7	48.6	51.3	54.2	57.1	59.8	62.7	4.3		47.6	49.4	51.1	52.9	54.7	56.4	58.2	2.7
5.6	5.9	6.2	6.5	6.9	7.2	7.5	0.5		5.8	6.1	6.4	6.7	6.9	7.2	7.5	0.4
14.2	15.0	15.8	16.6	17.4	18.2	19.0	1.2		14.7	15.5	16.2	16.9	17.6	18.3	19.1	1.1
2.6	3.3	3.9	4.5	5.2	5.8	6.5	1.0		3.2	3.6	4.0	4.4	4.9	5.3	5.7	0.6
6.5	8.3	9.8	11.5	13.2	14.7	16.5	2.5		8.1	9.2	10.2	11.3	12.4	13.4	14.5	1.6
6.9	7.6	8.1	8.8	9.4	10.0	10.7	0.9		7.6	8.0	8.4	8.8	9.2	9.5	10.0	0.6
17.5	19.2	20.7	22.3	23.9	25.4	27.1	2.4		19.3	20.4	21.3	22.3	23.3	24.2	25.3	1.5
								6 years								
36.2	39.7	42.8	46.3	49.8	52.9	56.4	5.1	Weight	32.8	37.0	41.0	45.4	49.8	53.8	58.0	6.4
16.4	18.0	19.4	21.0	22.6	24.0	25.6	2.32	Height	14.9	16.8	18.6	20.6	22.6	24.4	26.3	2.9
42.0	43.4	44.6	45.9	47.2	48.3	49.7	1.9	Sitting height	41.7	43.1	44.3	45.6	47.0	48.2	49.5	2.0
106.8	110.2	113.2	116.5	119.8	122.8	126.2	4.9	Shoulder width	106.0	10						

Boys								Girls							
95%								95%							
80%								80%							
50%								50%							
<i>P</i> ₁₀	<i>P</i> ₁₅	<i>P</i> ₂₅	<i>P</i> ₅₀	<i>P</i> ₇₅	<i>P</i> ₉₀	<i>P</i> ₉₅	<i>z</i>	<i>P</i> ₁₀	<i>P</i> ₁₅	<i>P</i> ₂₅	<i>P</i> ₅₀	<i>P</i> ₇₅	<i>P</i> ₉₀	<i>P</i> ₉₅	<i>z</i>
7 years								7 years							
43.7	47.2	51.1	55.1	58.6	62.6	67.6	5.8	34.8	40.6	45.9	51.8	57.8	63.1	68.8	8.6
19.8	21.4	23.2	25.0	26.6	28.4	29.8	2.61	13.8	15.4	16.8	18.2	19.6	21.0	22.4	1.8
45.6	46.8	48.2	49.6	50.8	52.2	53.6	2.0	43.9	45.4	46.7	48.2	49.6	51.0	52.5	2.2
115.8	118.9	122.4	125.9	129.0	132.3	135.1	3.1	111.3	115.3	118.7	122.4	126.1	129.5	133.3	5.5
23.7	24.5	25.3	26.1	26.8	27.6	28.1	1.2	22.7	23.5	24.3	25.1	25.9	26.7	27.5	1.2
60.3	62.2	64.2	66.2	68.1	70.1	71.0	3.0	37.6	39.7	41.6	43.7	45.8	47.7	49.8	3.1
9.6	10.1	10.6	11.0	11.5	11.7	11.7	0.7	8.8	9.4	9.9	10.5	11.1	11.6	12.2	0.9
24.5	25.6	26.8	28.0	29.1	29.8	30.8	1.8	22.3	23.9	25.2	26.7	28.2	29.5	31.1	2.2
7.2	7.7	8.2	8.7	9.2	9.7	9.7	0.7	6.9	7.4	7.8	8.3	8.7	9.2	9.7	0.7
18.4	19.6	20.9	22.2	23.4	24.7	25.9	1.9	17.4	18.7	19.8	21.0	22.2	23.3	24.6	1.8
18.9	19.6	20.3	21.0	21.7	22.4	23.1	1.1	18.5	19.1	19.6	20.2	20.7	21.2	21.8	0.8
48.1	49.8	51.6	53.4	55.1	56.9	58.7	2.7	47.0	48.5	49.8	51.2	52.6	53.9	55.4	2.1
20.9	21.5	22.2	23.0	23.6	24.3	25.1	1.1	19.0	20.0	20.8	21.7	22.7	23.5	24.4	1.4
53.0	54.7	56.5	58.3	60.0	61.8	63.6	2.7	48.3	50.7	52.8	55.2	57.6	59.7	62.1	3.5
6.1	6.5	6.8	7.1	7.4	7.7	7.7	0.5	5.7	6.2	6.6	7.0	7.4	7.8	8.3	0.6
15.6	16.4	17.2	18.0	18.8	19.6	20.4	1.6	14.6	15.7	16.7	17.8	18.9	19.9	21.0	1.6
3.9	4.3	4.8	5.2	5.6	6.0	6.0	0.6	3.7	4.0	4.3	4.7	5.0	5.4	5.7	0.5
10.0	11.0	12.1	13.2	14.2	15.3	16.4	1.6	9.3	10.2	11.0	11.9	12.8	13.6	14.5	1.3
8.1	8.7	9.3	10.0	10.5	11.1	11.7	0.9	8.1	8.6	9.0	9.5	10.0	10.4	10.9	0.7
20.7	22.1	23.7	25.3	26.7	28.3	29.3	2.3	20.5	21.8	22.9	24.1	25.3	26.4	27.7	1.8
7½ years								7½ years							
45.0	48.9	53.6	58.2	62.2	66.8	71.0	6.7	36.8	43.2	49.2	55.6	61.9	67.9	74.3	9.5
20.4	22.2	24.3	26.4	28.2	30.3	30.5	3.05	16.7	19.6	22.3	25.2	28.1	30.8	33.7	4.3
46.7	47.9	49.3	50.7	51.9	53.3	54.0	2.0	45.2	46.7	48.0	49.4	50.8	52.1	53.5	2.1
118.6	121.7	125.2	128.7	131.8	135.3	138.1	5.1								
24.1	24.9	25.7	26.5	27.2	28.0	28.1	1.2								
61.3	63.2	65.2	67.2	69.1	71.1	71.0	3.0								
9.9	10.4	10.8	11.3	11.7	12.0	12.0	0.7								
22.2	23.3	24.3	25.3	26.3	27.3	27.3	1.8								
7.4	7.9	8.3	8.8	9.3	9.8	9.8	0.7								
18.9	20.0	21.2	22.4	23.5	24.8	25.8	1.8								
19.0	19.6	20.4	21.1	21.7	22.4	23.1	1.1								
48.2	49.9	51.7	53.5	55.2	57.0	58.7	2.7								
21.1	21.8	22.6	23.3	24.1	24.8	25.5	1.1								
33.5	35.3	37.3	39.3	41.1	43.0	44.9	2.9								
6.2	6.5	6.9	7.3	7.6	8.0	8.6	0.6								
13.7	15.3	17.3	19.3	21.3	23.3	25.3	1.4								
4.1	4.4	4.8	5.2	5.6	5.9	6.6	0.6								
10.5	11.3	12.3	13.3	14.1	15.1	16.1	1.4								
8.3	8.9	9.5	10.2	10.7	11.3	11.9	0.9								
21.2	22.6	24.2	25.8	27.2	28.8	29.8	2.3								
8 years								8 years							
45.9	50.5	55.8	61.1	65.7	71.0	77.0	7.7	38.8	45.6	52.0	58.9	65.7	72.1	78.9	10.1
20.8	22.9	25.3	27.7	29.8	32.2	34.9	3.49	17.6	20.7	23.6	26.7	29.8	32.7	35.8	4.6
47.8	49.0	50.4	51.8	53.0	54.4	55.0	2.0	46.6	47.9	49.1	50.5	51.8	53.0	54.4	2.0
121.3	124.5	128.0	131.5	134.7	138.5	142.1	5.2	118.3	121.7	124.8	128.2	131.6	134.7	138.1	5.0
24.4	25.2	26.1	26.9	27.7	28.5	29.1	1.2	23.8	24.5	25.2	25.9	26.7	27.4	28.1	1.1
62.1	64.0	66.2	68.4	70.7	72.5	74.2	3.2	60.4	62.3	64.0	65.9	67.8	69.5	71.4	2.8
10.2	10.6	11.1	11.5	11.9	12.2	12.7	0.7	9.7	10.2	10.6	11.0	11.5	11.9	12.4	0.7
25.9	26.9	27.9	28.9	29.9	30.9	31.9	1.7	24.6	25.6	26.6	27.6	28.6	29.6	30.6	1.7
7.8	8.1	8.5	8.9	9.3	9.7	10.6	0.6	7.4	7.8	8.2	8.6	9.1	9.4	9.8	0.6
19.7	20.6	21.6	22.6	23.5	24.6	25.5	1.5	18.8	19.8	20.8	21.9	22.9	24.0	25.0	1.6
19.0	19.7	20.4	21.1	21.8	22.5	23.1	1.1	18.5	19.1	19.6	20.3	20.9	21.5	22.1	0.9
48.3	50.0	51.8	53.6	55.3	57.1	58.9	2.7	46.9	48.5	49.9	51.5	53.1	54.5	56.1	2.3
21.3	22.0	22.9	23.7	24.4	25.3	26.2	1.2	19.4	20.5	21.4	22.5	23.5	24.5	25.5	1.5
34.1	35.0	36.1	37.2	38.3	39.4	40.5	3.1	49.4	52.0	54.4	57.1	59.8	62.2	64.8	3.9
6.3	6.6	7.0	7.4	7.8	8.2	8.6	0.6	5.7	6.3	6.7	7.3	7.8	8.3	8.9	0.8
15.9	16.8	17.8	18.8	19.7	20.8	21.5	1.5	14.5	15.9	17.1	18.5	19.9	21.1	22.5	2.0
4.3	4.6	4.9	5.3	5.6	5.9	6.5	0.5	3.4	3.9	4.4	5.0	5.5	6.0	6.5	0.8
10.8	11.6	12.5	13.4	14.2	15.1	16.1	1.3	8.6	10.0	11.2	12.6	14.0	15.2	16.6	2.0
8.5	9.1	9.7	10.4	10.9	11.5	12.1	0.9	8.3	9.0	9.5	10.1	10.7	11.2	11.8	0.9
22.7	23.1	24.7	26.3	27.7	29.3	29.3	2.3	21.2	22.8	24.1	25.6	27.1	28.4	30.0	2.2

Normal Measurements During Growth - 8½ Years to 9½ Years'

Weight in pounds and kilograms; other measurements in inches and centimetres (*P* = percentile)

Boys								Girls								
95%								95%								
80%								80%								
50%								50%								
<i>P</i> _{1.5}	<i>P</i> ₁₀	<i>P</i> ₂₅	<i>P</i> ₅₀	<i>P</i> ₇₅	<i>P</i> ₉₀	<i>P</i> _{97.5}	<i>s</i>		<i>P</i> _{1.5}	<i>P</i> ₁₀	<i>P</i> ₂₅	<i>P</i> ₅₀	<i>P</i> ₇₅	<i>P</i> ₉₀	<i>P</i> _{97.5}	
								8½ years								
39.0	45.6	51.6	58.2	64.8	70.8	77.4	9.6	Weight	40.3	47.6	54.0	61.3	68.6	75.0	82.2	
17.7	20.7	23.4	26.4	29.4	32.1	35.1	4.37	Height	18.3	21.6	24.5	27.8	31.1	34.0	37.3	
47.5	48.9	50.1	51.5	52.8	54.1	55.4	2.0	Sitting height	47.5	48.9	50.1	51.5	52.9	54.1	55.5	
120.6	124.1	127.2	130.7	134.2	137.3	140.8	5.1	Shoulder width	120.7	124.2	127.3	130.8	134.3	137.4	140.9	
23.8	24.7	25.6	26.5	27.4	28.2	29.1	1.3	Pelvic width	24.3	25.0	25.7	26.4	27.1	27.8	28.5	
60.5	62.8	64.9	67.2	69.5	71.6	73.9	3.4	Head circ.	61.7	63.5	65.2	67.0	68.8	70.5	72.3	
9.8	10.5	10.9	11.3	11.7	12.1	12.3	0.6	Chest circ.	9.9	10.4	10.8	11.3	11.7	12.1	12.6	
24.9	26.6	27.6	28.7	29.8	30.8	31.3	1.6	Upper arm circ.	25.2	26.4	27.4	28.6	29.8	30.8	32.0	
7.6	8.0	8.3	8.7	9.0	9.3	9.7	0.5	Wrist circ.	7.6	8.0	8.3	8.8	9.2	9.6	10.0	
19.4	20.3	21.1	22.0	22.9	23.7	24.6	1.3	Calf circ.	19.2	20.2	21.2	22.3	23.4	24.4	25.4	
18.3	19.0	19.7	20.4	21.2	21.9	22.6	1.1		18.1	18.9	19.6	20.3	21.1	21.7	22.5	
46.4	48.3	50.0	51.9	53.8	55.5	57.4	2.8		46.1	48.0	49.7	51.6	53.5	55.2	57.1	
20.7	21.6	22.4	23.2	24.1	24.8	25.7	1.3		19.5	20.7	21.7	22.8	23.9	24.9	26.1	
52.7	54.9	56.8	59.0	61.2	63.1	65.3	3.2		49.6	52.5	55.0	57.9	60.8	63.3	66.2	
5.9	6.4	6.7	7.1	7.5	7.9	8.3	0.6		5.7	6.3	6.9	7.4	8.0	8.5	9.1	
15.1	16.2	17.1	18.1	19.1	20.0	21.1	1.5		14.6	16.1	17.4	18.8	20.2	21.5	23.0	
4.0	4.3	4.6	5.0	5.4	5.7	6.0	0.5		3.7	4.1	4.5	5.0	5.5	5.9	6.3	
10.1	11.0	11.8	12.7	13.6	14.4	15.3	1.3		9.3	10.5	11.5	12.7	13.9	14.9	16.1	
8.1	8.7	9.3	9.9	10.6	11.1	11.7	0.9		8.4	9.0	9.6	10.2	10.8	11.4	12.0	
20.6	22.2	23.6	25.2	26.8	28.2	29.8	2.3		21.3	22.9	24.3	25.9	27.5	28.9	30.5	
								9 years								
41.2	47.8	54.0	60.6	67.2	73.4	80.0	9.8	Weight	42.5	49.8	56.2	63.5	70.8	77.2	84.4	
18.7	21.7	24.5	27.5	30.5	33.3	36.3	4.46	Height	19.3	22.6	25.5	28.8	32.1	35.0	38.3	
48.5	49.9	51.1	52.5	53.9	55.1	56.5	2.0	Sitting height	48.4	49.8	51.1	52.4	53.8	55.1	56.5	
123.2	126.7	129.8	133.3	136.8	139.9	143.4	5.1	Shoulder width	122.9	126.5	129.7	133.2	136.7	139.9	143.5	
23.9	24.9	25.8	26.8	27.8	28.7	29.7	1.5	Pelvic width	24.4	25.2	25.9	26.8	27.6	28.3	29.2	
60.8	63.3	65.6	68.1	70.6	72.9	75.4	3.7	Head circ.	61.9	64.0	65.9	68.0	70.1	72.0	74.1	
10.0	10.7	11.1	11.5	12.0	12.4	12.6	0.6	Chest circ.	10.0	10.6	11.0	11.5	11.9	12.4	12.9	
25.5	27.2	28.2	29.3	30.4	31.4	31.9	1.6	Upper arm circ.	25.5	26.8	27.9	29.1	30.3	31.4	32.7	
7.9	8.2	8.5	8.8	9.1	9.4	9.8	0.5	Wrist circ.	7.7	8.1	8.5	8.9	9.4	9.8	10.2	
20.0	20.8	21.6	22.4	23.2	24.0	24.8	1.2	Calf circ.	19.6	20.6	21.6	22.7	23.8	24.8	25.8	
18.3	19.1	19.7	20.5	21.2	21.9	22.6	1.1		17.8	18.7	19.5	20.4	21.3	22.1	23.0	
46.5	48.4	50.1	52.0	53.9	55.6	57.5	2.8		45.1	47.4	49.5	51.8	54.1	56.2	58.5	
21.2	22.1	22.8	23.7	24.6	25.3	26.2	1.3		19.3	20.6	21.8	23.1	24.4	25.6	26.9	
53.9	56.1	58.0	60.2	62.4	64.3	66.5	3.2		48.9	52.3	55.3	58.6	61.9	64.9	68.3	
6.1	6.5	6.9	7.2	7.6	8.0	8.3	0.6		5.8	6.4	6.9	7.5	8.1	8.6	9.3	
15.6	16.6	17.4	18.4	19.4	20.2	21.2	1.4		14.7	16.3	17.6	19.1	20.6	21.9	23.5	
4.1	4.4	4.8	5.1	5.4	5.7	6.0	0.5		3.9	4.3	4.6	5.0	5.4	5.7	6.1	
10.5	11.3	12.1	12.9	13.7	14.5	15.3	1.2		9.9	10.9	11.7	12.7	13.7	14.5	15.5	
8.3	8.9	9.4	10.1	10.7	11.3	11.9	0.9		8.4	9.1	9.7	10.3	10.9	11.5	12.2	
21.0	22.6	24.0	25.6	27.2	28.6	30.2	2.3		21.4	23.1	24.6	26.2	27.8	29.3	31.0	
								9½ years								
41.9	49.2	55.8	63.1	70.3	76.9	84.2	10.7	Weight	45.2	52.5	58.9	66.1	73.4	79.8	87.1	
19.0	22.3	25.3	28.6	31.9	34.9	38.2	4.86	Height	20.5	23.8	26.7	30.0	33.3	36.2	39.5	
49.3	50.7	52.0	53.5	54.9	56.2	57.6	2.1	Sitting height	49.1	50.6	51.9	53.3	54.8	56.1	57.5	
125.3	128.9	132.2	135.8	139.4	142.7	146.3	5.3	Shoulder width	124.7	128.4	131.7	135.4	139.1	142.4	146.1	
24.0	25.1	26.1	27.2	28.3	29.3	30.4	1.6	Pelvic width	24.0	25.1	26.1	27.2	28.3	29.3	30.4	
61.0	63.8	66.3	69.1	71.9	74.4	77.2	4.1	Head circ.	61.0	63.8	66.3	69.1	71.9	74.4	77.2	
10.5	10.9	11.3	11.8	12.2	12.6	13.0	0.6	Chest circ.	10.1	10.6	11.1	11.6	12.1	12.6	13.1	
26.7	27.8	28.8	29.9	31.0	32.0	33.1	1.6	Upper arm circ.	25.7	27.0	28.2	29.5	30.8	32.0	33.3	
8.0	8.3	8.6	9.0	9.3	9.6	10.0	0.5	Wrist circ.	7.9	8.3	8.7	9.1	9.5	9.9	10.3	
20.2	21.1	21.9	22.8	23.7	24.5	25.4	1.3	Calf circ.	20.0	21.0	22.0	23.1	24.2	25.2	26.2	
18.3	19.1	19.8	20.5	21.3	21.9	22.7	1.1		17.5	18.5	19.4	20.4	21.5	22.4	23.4	
46.6	48.5	50.2	52.1	54.0	55.7	57.6	2.8		44.4	47.0	49.3	51.9	54.5	56.8	59.4	
21.7	22.5	23.3	24.1	25.0	25.7	26.6	1.3		19.1	20.6	21.9	23.4	24.8	26.2	27.7	
55.0	57.2	59.1	61.3	63.5	65.4	67.6	3.2		48.5	52.3	55.7	59.4	63.1	66.5	70.3	
6.3	6.7	7.0	7.4	7.8	8.1	8.5	0.6		5.8	6.5	7.0	7.6	8.3	8.8	9.4	
15.9	16.9	17.7	18.7	19.7	20.5	21.5	1.4		14.8	16.4	17.8	19.4	21.0	22.4	24.0	
4.2	4.5	4.8	5.2	5.5	5.8	6.1	0.5		3.9	4.3	4.7	5.1	5.5	5.8	6.3	
10.7	11.5	12.3	13.1	13.9	14.7	15.5	1.2		9.9	11.0	11.9	12.9	13.9	14.8	15.9	
8.5	9.1	9.6	10.3	10.9	11.5	12.1	0.9		8.6	9.3	9.8	10.5	11.1	11.7	12.4	
21.5	23.1	24.5	26.1	27.7	29.1	30.7	2.3		21.8	23.5	25.0	26.6	28.2	29.7	31.4	

701

Boys										Girls																				
95%										95%																				
80%										80%																				
50%										50%																				
P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₅	P _{97.5}	P ₉₉	P _{99.5}	P ₁₀₀	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₅	P _{97.5}	P ₉₉	P _{99.5}	P ₁₀₀											
10 years																														
Weight										46.7	54.7	61.7	69.4	77.2	84.2	92.2	11.5													
Height										21.2	24.8	28.0	31.5	35.0	38.2	41.8	5.2													
Sitting height										49.8	51.3	52.6	54.1	55.6	57.0	58.5	2.2													
Shoulder width																				1.9										
Pelvic width																				0.8										
Head circ.																				0.7										
Chest circ.																				1.7										
Upper arm circ.																				1.6										
Wrist circ.																				1.0										
Calf circ.																				0.9										
10½ years																														
Weight										47.0	56.0	65.9	72.8	81.6	89.5	98.5	13.0													
Height										21.3	25.4	29.0	33.0	37.0	40.6	44.7	5.9													
Sitting height										50.2	51.8	53.3	54.9	56.6	58.0	59.7	2.4													
Shoulder width										127.4	131.6	135.3	139.5	145.7	147.4	151.4	6.1													
Pelvic width										24.0	25.4	26.7	28.1	29.4	30.7	32.1	2.0													
Head circ.										61.0	64.6	67.8	71.5	74.8	78.0	81.6	5.2													
Chest circ.										10.3	10.9	11.4	12.0	12.6	13.1	13.7	0.8													
Upper arm circ.										26.2	27.7	29.0	30.5	32.0	33.5	34.8	2.1													
Wrist circ.										8.0	8.5	9.0	9.4	9.9	10.4	10.9	0.7													
Calf circ.										20.4	21.7	22.8	24.0	25.2	26.5	27.6	1.8													
Weight										17.4	18.5	19.4	20.6	21.7	22.6	23.7	1.6													
Height										44.1	46.9	49.4	52.2	55.0	57.6	60.3	4.1													
Sitting height										19.3	20.9	22.4	24.0	25.6	27.0	28.7	2.4													
Shoulder width										49.0	53.1	56.8	60.9	65.0	68.7	72.8	6.0													
Pelvic width										5.9	6.6	7.2	7.9	8.6	9.3	9.9	1.0													
Head circ.										15.0	16.7	18.3	20.1	21.9	23.5	25.2	2.6													
Chest circ.										3.2	3.9	4.6	5.3	6.0	6.7	7.4	1.1													
Upper arm circ.										8.1	9.9	11.6	13.4	15.2	16.9	18.7	2.7													
Wrist circ.										8.8	9.5	10.2	10.9	11.7	12.4	13.1	1.1													
Calf circ.										22.3	24.2	25.9	27.8	29.7	31.4	33.3	2.8													
11 years																														
Weight										48.3	58.2	67.0	76.7	86.4	95.2	105.2	14.3													
Height										21.9	26.4	30.4	34.8	39.2	43.2	47.7	6.5													
Sitting height										50.7	52.5	54.1	55.8	57.6	59.1	60.9	2.6													
Shoulder width										128.9	133.4	137.4	141.8	146.2	150.2	154.7	6.5													
Pelvic width										24.3	25.7	27.0	28.5	30.0	31.3	32.7	2.1													
Head circ.										61.7	65.4	68.7	72.4	76.1	79.4	83.1	5.4													
Chest circ.										10.4	11.0	11.6	12.2	12.8	13.4	14.0	0.9													
Upper arm circ.										26.4	28.0	29.4	31.0	32.6	34.0	35.6	2.3													
Wrist circ.										8.1	8.7	9.1	9.6	10.2	10.6	11.1	0.7													
Calf circ.										20.7	22.2	23.2	24.5	25.8	26.8	28.3	1.9													

Normal Measurements During Growth - 11 ½ Years to 12 ½ Years¹

Weight in pounds and kilogrammes; other measurements in inches and centimetres (*P* = percentile)

Boys								Girls								
95%								95%								
80%								80%								
50%								50%								
<i>P</i> _{2.5}	<i>P</i> ₁₀	<i>P</i> ₂₅	<i>P</i> ₅₀	<i>P</i> ₇₅	<i>P</i> ₉₀	<i>P</i> _{97.5}	<i>s</i>		<i>P</i> _{2.5}	<i>P</i> ₁₀	<i>P</i> ₂₅	<i>P</i> ₅₀	<i>P</i> ₇₅	<i>P</i> ₉₀	<i>P</i> _{97.5}	<i>s</i>
								11½ years								
53.6	63.5	72.3	82.2	92.2	101.0	110.9	14.5	Weight	50.5	61.1	70.5	81.1	91.7	101.2	111.8	15.4
24.3	28.8	32.8	37.3	41.8	45.8	50.3	6.59	Height	22.9	27.7	32.0	36.8	41.6	45.9	50.7	7.0
52.0	53.7	55.2	57.0	58.7	60.2	62.0	2.5	Sitting height	51.5	53.4	55.1	57.0	58.9	60.6	62.6	2.8
132.0	136.4	140.3	144.7	149.1	153.0	157.4	6.4	Shoulder width	130.7	135.6	140.0	144.8	149.6	154.0	158.9	7.1
24.8	26.2	27.4	28.8	30.2	31.4	32.8	2.0	Pelvic width	25.0	26.3	27.6	28.9	30.3	31.5	32.9	2.0
63.0	66.5	69.6	73.1	76.6	79.7	83.2	5.1	Head circ.	63.4	66.9	70.0	73.5	77.0	80.1	83.6	5.1
10.8	11.5	12.0	12.6	13.3	13.8	14.4	0.9	Chest circ.	10.6	11.2	11.8	12.4	13.1	13.7	14.3	0.9
27.5	29.1	30.5	32.1	33.7	35.1	36.7	2.3	Upper arm circ.	26.8	28.5	30.0	31.6	33.2	34.7	36.4	2.4
7.8	8.5	9.1	9.7	10.3	10.9	11.6	0.9	Wrist circ.	8.3	8.9	9.3	9.9	10.4	10.8	11.5	0.8
19.8	21.5	23.0	24.6	26.2	27.7	29.4	2.4	Calf circ.	21.1	22.7	23.7	25.1	26.5	27.5	29.1	2.0
19.3	19.8	20.2	20.7	21.2	21.6	22.1	0.7		18.2	19.1	19.8	20.6	21.5	22.2	23.0	1.2
49.0	50.3	51.4	52.6	53.8	54.9	56.2	1.8		46.3	48.4	50.3	52.4	54.5	56.4	58.5	3.1
21.9	23.0	24.1	25.3	26.5	27.5	28.7	1.7		19.7	21.4	22.9	24.6	26.2	27.7	29.4	2.4
55.5	58.5	61.2	64.2	67.2	69.9	72.9	4.4		50.1	54.4	58.2	62.4	66.6	70.4	74.7	6.2
6.2	6.8	7.4	8.0	8.6	9.2	9.8	0.9		6.1	6.8	7.4	8.1	8.9	9.5	10.2	1.0
15.7	17.3	18.7	20.3	21.9	23.3	24.9	2.3		15.5	17.3	18.9	20.7	22.5	24.1	25.9	2.6
3.9	4.4	4.9	5.4	5.9	6.4	6.9	0.7		4.6	4.8	5.1	5.4	5.6	5.9	6.1	0.4
9.9	11.2	12.4	13.7	15.0	16.2	17.5	1.9		11.6	12.3	12.9	13.6	14.3	14.9	15.6	1.0
9.1	9.8	10.4	11.0	11.7	12.2	12.9	0.9		8.9	9.7	10.4	11.2	12.0	12.7	13.4	1.1
23.2	24.9	26.4	28.0	29.6	31.1	32.8	2.4		22.7	24.6	26.4	28.4	30.4	32.2	34.1	2.9
								12 years								
56.9	67.5	76.7	87.1	97.4	106.7	117.3	15.2	Weight	53.6	64.8	75.0	86.0	97.0	107.1	118.4	16.3
25.8	30.6	34.8	39.5	44.2	48.4	53.2	6.91	Height	24.3	29.4	34.0	39.0	44.0	48.6	53.7	7.4
52.6	54.4	56.1	57.9	59.7	61.3	63.2	2.7	Sitting height	52.6	54.6	56.4	58.5	60.5	62.3	64.4	3.0
133.5	138.2	142.4	147.0	151.6	155.8	160.5	6.8	Shoulder width	133.5	138.7	143.3	148.5	153.7	158.5	163.5	7.6
25.4	26.7	27.9	29.2	30.5	31.6	32.9	1.9	Pelvic width	25.6	26.9	28.1	29.4	30.7	31.8	33.1	1.9
64.6	67.9	70.8	74.1	77.4	80.3	83.6	4.8	Head circ.	65.1	68.4	71.3	74.6	77.9	80.8	84.1	4.8
10.5	11.3	12.0	12.8	13.6	14.3	15.1	1.2	Chest circ.	10.7	11.5	12.0	12.7	13.4	14.0	14.7	1.0
26.6	28.6	30.5	32.5	34.5	36.4	38.4	3.0	Upper arm circ.	27.3	29.1	30.6	32.3	34.0	35.5	37.3	2.5
7.6	8.4	9.1	9.9	10.7	11.4	12.1	1.1	Wrist circ.	8.5	9.2	9.6	10.2	10.7	11.2	11.9	0.8
19.4	21.3	23.1	25.1	27.1	28.9	30.8	2.9	Calf circ.	21.7	23.4	24.5	25.9	27.3	28.4	30.1	2.1
19.4	19.9	20.3	20.7	21.2	21.6	22.1	0.7		19.0	19.6	20.1	20.7	21.2	21.7	22.3	0.8
49.3	50.5	51.5	52.7	53.9	54.9	56.1	1.7		48.3	49.8	51.1	52.5	53.9	55.2	56.7	2.1
22.1	23.3	24.4	25.6	26.8	27.9	29.1	1.8		19.9	21.6	23.1	24.8	26.5	28.1	29.8	2.5
56.1	59.2	61.9	65.0	68.1	70.8	73.9	4.5		50.6	54.9	58.8	63.1	67.4	71.3	75.6	6.3
6.0	6.7	7.4	8.1	8.9	9.6	10.3	1.1		6.2	6.9	7.6	8.3	9.0	9.6	10.3	1.0
15.2	17.1	18.8	20.7	22.6	24.3	26.2	2.8		15.8	17.6	19.2	21.0	22.8	24.4	26.2	2.6
3.6	4.2	4.8	5.4	6.0	6.6	7.2	0.9		4.6	4.9	5.2	5.4	5.7	5.9	6.2	0.4
9.1	10.7	12.1	13.7	15.3	16.7	18.3	2.3		11.8	12.5	13.1	13.8	14.5	15.1	15.8	1.0
9.3	10.0	10.6	11.2	11.9	12.4	13.1	0.9		9.1	9.8	10.5	11.3	12.1	12.8	13.5	1.1
23.7	25.4	26.9	28.5	30.1	31.6	33.3	2.4		23.0	24.9	26.7	28.7	30.7	32.5	34.4	2.9
								12½ years								
59.3	70.8	80.9	92.2	103.4	113.5	125.0	16.5	Weight	56.9	68.8	79.4	91.3	103.2	113.8	125.7	17.4
26.9	32.1	36.7	41.8	46.9	51.5	56.7	7.50	Height	25.8	31.2	36.0	41.4	46.8	51.6	57.0	7.9
53.3	55.3	57.1	59.1	61.0	62.8	64.8	2.9	Sitting height	53.7	55.7	57.6	59.6	61.7	63.6	65.6	3.0
135.3	140.4	145.0	150.0	155.0	159.6	164.7	7.4	Shoulder width	136.3	141.5	146.3	151.5	156.7	161.5	166.7	7.7
26.1	27.3	28.4	29.6	30.7	31.8	33.0	1.7	Pelvic width	26.5	27.6	28.7	29.8	30.9	32.0	33.1	1.7
66.4	69.4	72.1	75.1	78.1	80.8	83.8	4.4	Head circ.	67.2	70.1	72.8	75.7	78.6	81.3	84.2	4.3
9.5	10.7	11.7	12.9	14.0	15.1	16.2	1.7	Chest circ.	11.0	11.7	12.3	13.0	13.6	14.2	14.9	1.0
24.2	27.1	29.8	32.7	35.6	38.3	41.2	4.3	Upper arm circ.	27.9	29.7	31.2	32.9	34.6	36.1	37.9	2.5
7.6	8.4	9.3	10.1	11.0	11.8	12.7	1.3	Wrist circ.	8.8	9.5	10.0	10.6	11.1	11.6	12.3	0.9
19.2	21.4	23.5	25.7	27.9	30.0	32.2	3.3	Calf circ.	22.4	24.2	25.3	26.8	28.3	29.4	31.2	2.2
19.5	20.0	20.4	20.8	21.2	21.6	22.0	0.6		19.4	19.9	20.3	20.7	21.2	21.6	22.1	0.7
49.6	50.7	51.7	52.8	53.9	54.9	56.0	1.6		49.3	50.5	51.5	52.7	53.9	54.9	56.1	1.7
22.3	23.6	24.8	26.1	27.4	28.5	29.8	1.9		20.2	21.9	23.5	25.2	26.9	28.5	30.2	2.5
56.7	60.0	62.9	66.2	69.5	72.4	75.7	4.8		51.3	55.7	59.6	64.0	68.4	72.3	76.6	6.4
5.7	6.6	7.4	8.3	9.1	10.0	10.8	1.3		6.3	7.0	7.7	8.4	9.1	9.7	10.4	1.0
14.5	16.7	18.8	21.0	23.2	25.3	27.5	3.3		16.1	17.9	19.5	21.3	23.1	24.7	26.5	2.6
3.5	4.2	4.8	5.4	6.1	6.7	7.4	1.0		4.8	5.0	5.3	5.6	5.8	6.1	6.3	0.4
8.8	10.6	12.1	13.8	15.5	17.0	18.8	2.5		12.1	12.8	13.4	14.1	14.8	15.4	16.1	1.0
9.3	10.0	10.7	11.4	12.1	12.8	13.5	1.1		9.3	10.0	10.7	11.5	12.3	13.0	13.7	1.1
23.7	25.5	27.2	29.0	30.8	32.5	34.3	2.7		23.5	25.4	27.2	29.2	31.2	33.0	34.9	2.6

Weight in pounds and kilograms, other measurements in inches and centimetres (P = percentile)

Boys							Girls						
95%							95%						
80%							80%						
50%							50%						
P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₅	s	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P ₉₅	s
13 years													
75.4	85.8	97.2	108.7	119.1	130.7	16.9							
34.2	38.9	44.1	49.3	54.0	59.3	7.67							
56.4	58.3	60.4	62.5	64.4	66.5	3.1							
						7.8							
						4.3							
						2.0							
						3.5							
8.4	9.3	10.4	11.4	12.3	13.1	1.5							
21.4	23.7	26.3	28.9	31.2	33.3	3.8							
20.1	20.4	20.8	21.2	21.6	22.0	0.6							
51.0	51.9	52.9	53.9	54.8	55.9	1.5							
23.4	24.9	26.5	28.2	29.6	31.3	2.4							
59.5	63.2	67.4	71.6	75.3	79.5	6.1							
6.7	7.5	8.3	9.2	10.0	10.9	1.3							
16.9	19.0	21.2	23.4	25.5	27.7	3.3							
4.3	4.9	5.6	6.2	6.8	7.5	1.0							
10.9	12.4	14.1	15.8	17.3	19.1	2.5							
9.8	10.6	11.6	12.5	13.3	14.3	1.4							
24.9	27.0	29.4	31.8	33.9	36.3	3.5							
13½ years													
79.8	90.4	102.1	113.8	124.3	136.2	17.2							
36.2	41.0	46.3	51.6	56.4	61.8	7.81							
57.7	59.7	61.8	63.9	65.9	68.0	3.1							
146.6	151.6	157.0	162.4	167.4	172.8	8.0							
28.4	29.5	30.6	31.8	32.8	34.0	1.7							
72.2	74.9	77.8	80.7	83.4	86.3	4.3							
11.3	12.3	13.4	14.6	15.6	16.3	1.7							
29.7	31.2	34.1	37.0	39.3	41.4	4.2							
8.9	9.7	10.6	11.6	12.4	13.3	1.4							
22.3	24.6	27.0	29.4	31.8	33.9	3.3							
20.1	20.5	20.9	21.3	21.6	22.0	0.6							
51.1	52.0	53.0	54.0	54.9	56.0	1.5							
23.4	25.2	27.2	29.3	31.1	33.1	3.0							
59.4	64.0	69.2	74.4	79.0	84.2	7.6							
7.0	7.7	8.5	9.2	9.9	10.6	1.1							
10.7	11.9	12.6	13.5	14.4	15.2	2.8							
9.4	10.5	11.5	12.5	13.5	14.5	0.9							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1							
9.1	10.2	11.2	12.2	13.2	14.2	1.1						</	

* HIRSHENBERG, J. *Hispanic Acta* 19 suppl 13 (1964). From measurements made in the period 1956-1957 on 2150 boys and 2150 girls in m...

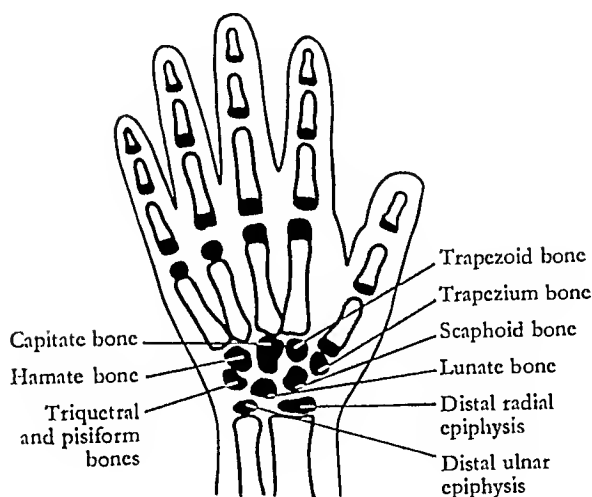
Normal Measurements During Growth - 14½ Years to 15½ Years¹

Weight in pounds and kilograms; other measurements in inches and centimetres (P = percentile)

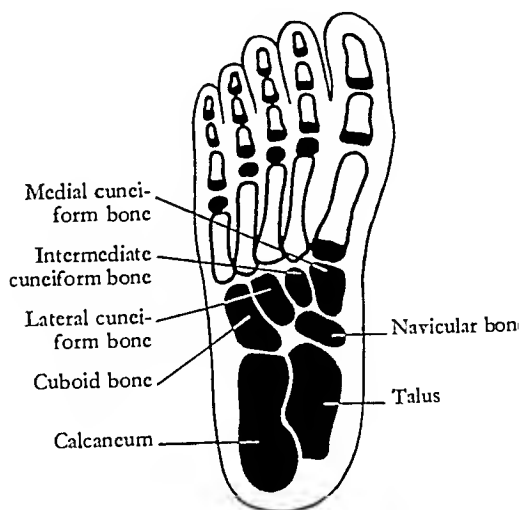
Boys								Girls							
95%								95%							
80%								80%							
50%								50%							
P _{2.5}	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P _{97.5}	r	P _{2.5}	P ₁₀	P ₂₅	P ₅₀	P ₇₅	P ₉₀	P _{97.5}	
14½ years															
75.6	88.4	99.6	112.2	124.8	136.0	148.8	18.5	Weight	81.3	92.8	103.0	114.2	125.4	135.6	147.0
34.3	40.1	45.2	50.9	56.6	61.7	67.5	8.37	Height	36.9	42.1	46.7	51.8	56.9	61.5	66.7
58.3	60.5	62.4	64.5	66.6	68.5	70.6	3.1	Sitting height	58.9	60.0	61.4	62.9	64.4	65.8	66.9
148.2	153.6	158.4	163.8	169.2	174.0	179.4	7.9	Shoulder width	149.7	152.5	156.0	159.8	163.6	167.1	169.9
28.4	29.6	30.6	31.8	33.0	34.1	35.2	1.7	Pelvic width	29.0	29.8	30.7	31.5	32.4	33.2	34.1
72.1	75.1	77.8	80.8	83.8	86.5	89.5	4.4	Head circ.	73.6	75.8	77.9	80.1	82.3	84.4	86.6
12.5	13.1	13.7	14.4	15.0	15.6	16.3	0.9	Chest circ.	12.2	12.8	13.4	14.0	14.6	15.2	15.8
31.7	33.4	34.9	36.5	38.1	39.6	41.3	2.4	Upper arm circ.	31.0	32.6	34.0	35.6	37.2	38.6	40.2
9.8	10.4	10.9	11.4	12.0	12.5	13.1	0.8	Wrist circ.	10.3	10.8	11.3	11.8	12.3	12.8	13.3
24.8	26.3	27.6	29.0	30.4	31.7	33.2	2.1	Calf circ.	26.1	27.4	28.6	29.9	31.2	32.4	33.7
19.8	20.2	20.6	21.0	21.4	21.7	22.2	0.6	Weight	19.8	20.2	20.6	21.0	21.5	21.9	22.3
50.3	51.4	52.3	53.3	54.3	55.2	56.3	1.5	Height	50.2	51.3	52.3	53.4	54.5	55.5	56.6
24.2	25.7	27.0	28.5	30.0	31.3	32.8	2.2	Sitting height	21.7	23.4	25.0	26.7	28.3	29.9	31.6
61.5	65.3	68.7	72.4	76.1	79.5	83.3	5.5	Shoulder width	55.2	59.5	63.4	67.7	72.0	75.9	80.2
7.4	8.0	8.4	8.9	9.4	9.9	10.4	0.7	Pelvic width	7.2	7.8	8.3	8.9	9.4	10.0	10.6
18.9	20.2	21.4	22.7	24.0	25.2	26.5	1.9	Head circ.	18.4	19.9	21.2	22.6	24.0	25.3	26.8
4.8	5.2	5.6	6.0	6.5	6.9	7.3	0.6	Chest circ.	-	-	-	5.7	-	-	-
12.1	13.2	14.2	15.3	16.4	17.4	18.5	1.6	Upper arm circ.	-	-	-	14.5	-	-	-
10.6	11.3	11.9	12.6	13.3	13.9	14.6	1.0	Wrist circ.	-	-	-	-	-	-	-
27.0	28.8	30.3	32.0	33.7	35.2	37.0	2.5	Calf circ.	10.4	11.1	11.9	12.6	13.4	14.1	14.9
15 years															
81.1	93.7	104.7	117.1	129.4	140.4	153.0	18.1	Weight	87.1	97.7	106.9	117.3	127.6	136.9	147.5
36.8	42.5	47.5	53.1	58.7	63.7	69.4	8.22	Height	39.5	44.3	48.5	53.2	57.9	62.1	66.9
59.8	61.9	63.7	65.7	67.7	69.5	71.5	3.0	Sitting height	59.4	60.6	61.9	63.4	64.9	66.3	67.4
151.9	157.1	161.7	166.8	171.9	176.5	181.7	7.5	Shoulder width	151.0	153.8	157.3	161.1	164.9	168.4	171.2
28.9	30.1	31.1	32.4	33.6	34.6	35.9	1.8	Pelvic width	29.5	30.4	31.1	32.0	32.8	33.6	34.4
73.3	76.4	79.1	82.2	85.3	88.0	91.1	4.5	Head circ.	74.9	77.1	79.0	81.2	83.4	85.3	87.5
13.0	13.6	14.1	14.7	15.3	15.8	16.5	0.9	Chest circ.	12.4	13.1	13.6	14.2	14.8	15.3	15.9
33.0	34.6	35.9	37.4	38.9	40.2	41.8	2.2	Upper arm circ.	31.6	33.2	34.5	36.0	37.5	38.8	40.4
10.0	10.6	11.1	11.7	12.2	12.8	13.3	0.8	Wrist circ.	10.5	10.9	11.4	11.9	12.4	12.9	13.3
25.5	27.0	28.3	29.7	31.1	32.4	33.9	2.1	Calf circ.	26.6	27.7	28.9	30.2	31.5	32.7	33.8
19.8	20.3	20.6	21.0	21.4	21.8	22.2	0.6	Weight	19.9	20.3	20.7	21.1	21.5	21.8	22.2
50.4	51.5	52.4	53.4	54.4	55.3	56.4	1.5	Height	50.5	51.6	52.5	53.5	54.5	55.4	56.5
25.2	26.5	27.8	29.1	30.4	31.7	33.0	2.0	Sitting height	22.1	23.8	25.2	26.9	28.5	30.0	31.7
64.0	67.4	70.5	73.9	77.3	80.4	83.8	5.0	Shoulder width	56.2	60.4	64.1	68.3	72.5	76.2	80.4
7.6	8.1	8.6	9.2	9.7	10.2	10.7	0.8	Pelvic width	7.4	8.0	8.5	9.0	9.6	10.0	10.6
19.3	20.7	21.9	23.3	24.7	25.9	27.3	2.0	Head circ.	18.9	20.3	21.5	22.9	24.3	25.5	26.9
5.1	5.4	5.7	6.1	6.5	6.8	7.1	0.5	Chest circ.	-	-	-	5.7	-	-	-
12.9	13.8	14.6	15.5	16.4	17.2	18.1	1.3	Upper arm circ.	-	-	-	14.5	-	-	-
11.0	11.7	12.2	12.9	13.5	14.1	14.8	0.9	Wrist circ.	-	-	-	-	-	-	-
27.9	29.6	31.1	32.7	34.3	35.8	37.5	2.4	Calf circ.	10.7	11.4	12.0	12.7	13.4	14.1	14.7
15½ years															
86.9	99.0	110.0	122.1	134.3	145.3	157.4	17.8	Weight	90.4	100.5	109.6	119.7	129.9	138.9	149.0
39.4	44.9	49.9	55.4	60.9	65.9	71.4	8.09	Height	41.0	45.6	49.7	54.3	58.9	63.0	67.6
61.3	63.2	64.9	66.7	68.6	70.2	72.1	2.7	Sitting height	59.3	60.9	62.2	63.8	65.4	66.8	68.3
155.8	160.6	164.8	169.5	174.2	178.4	183.2	6.9	Shoulder width	150.6	154.6	158.1	162.1	166.1	169.6	173.6
29.5	30.7	31.8	33.0	34.1	35.2	36.4	1.7	Pelvic width	29.9	30.8	31.5	32.4	33.3	34.0	34.9
75.0	78.0	80.7	83.7	86.7	89.4	92.4	4.4	Head circ.	76.0	78.2	80.1	82.3	84.5	86.4	88.6
13.1	14.0	14.5	15.0	15.6	16.1	16.4	0.8	Chest circ.	12.6	13.2	13.7	14.3	14.8	15.3	15.9
33.2	35.5	36.8	38.2	39.6	40.9	41.6	2.1	Upper arm circ.	32.0	33.5	34.8	36.2	37.6	38.9	40.4
10.3	10.9	11.4	11.9	12.5	13.0	13.6	0.8	Wrist circ.	10.6	11.1	11.5	12.0	12.5	12.9	13.4
26.1	27.6	28.9	30.3	31.7	33.0	34.5	2.1	Calf circ.	26.9	28.2	29.3	30.5	31.7	32.8	34.1
20.0	20.4	20.7	21.1	21.5	21.8	22.2	0.6	Weight	20.0	20.4	20.7	21.1	21.5	21.9	22.2
50.7	51.7	52.5	53.5	54.5	55.3	56.3	1.4	Height	50.9	51.9	52.7	53.7	54.7	55.5	56.5
25.9	27.2	28.3	29.6	30.9	32.0	33.3	1.9	Sitting height	22.6	24.1	25.5	27.1	28.7	30.0	31.6
65.9	69.1	72.0	75.2	78.4	81.3	84.5	4.7	Shoulder width	57.3	61.3	64.8	68.8	72.8	76.3	80.3
7.6	8.2	8.7	9.3	9.9	10.4	11.0	0.9	Pelvic width	7.8	8.3	8.7	9.2	9.6	10.1	10.6
19.2	20.8	22.1	23.6	25.1	26.4	28.0	2.2	Head circ.	19.7	21.0	22.1	23.3	24.5	25.6	26.9
5.3	5.6	5.9	6.1	6.4	6.7	7.0	0.4	Chest circ.	-	-	-	5.7	-	-	-
13.4	14.2	14.9	15.6	16.3	17.0	17.8	1.1	Upper arm circ.	-	-	-	14.5	-	-	-
11.2	11.9	12.4	13.0	13.7	14.2	14.8	0.9	Wrist circ.	-	-	-	-	-	-	-
28.5	30.1	31.5	33.1	34.7	36.1	37.7	2.3	Calf circ.	10.9	11.6	12.2	12.8	13.4	14.0	14.7

¹ HEIMENDINGER, J., *Helv. paediat. Acta*, 19, suppl. 13 (1964). From measurements made in the period 1956-1957 on 2150 boys and 2150 girls in Basel.

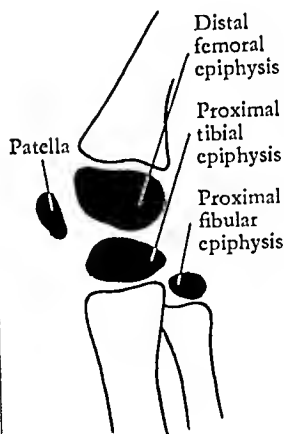
HAND AND WRIST



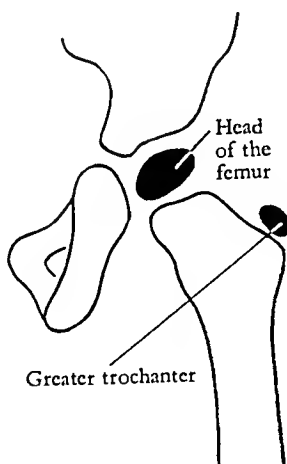
FOOT



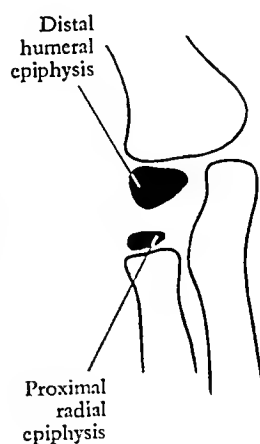
KNEE



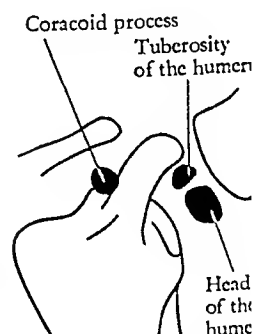
HIP



ELBOW



SHOULDER



In many clinical situations the assessment of skeletal development is a matter of considerable importance. Various regional ossification processes occurring between birth and maturity can be utilized for this purpose.

For routine clinical purposes the following indications constitute a reliable guide to skeletal development.

Newborn

In the full-term infant, knee X-rays (anteroposterior or lateral) should reveal a distinct and well-formed distal femoral epiphysis.

Bone age in childhood¹⁻⁶

The extent to which regional epiphyses are early or late in appearing can be determined by means of the table on page 707. In

* The data on pages 706-708 have been compiled in collaboration with H.J. KAUFMANN, Children's Hospital, Basle.

doing so it must be borne in mind that the range of physiological variation is rather wide, and that a discordance in the appearance of various ossification centres is commonly met. For this reason, diagnostic X-rays should include several regions of the body (wrist, knee and foot, possibly others).

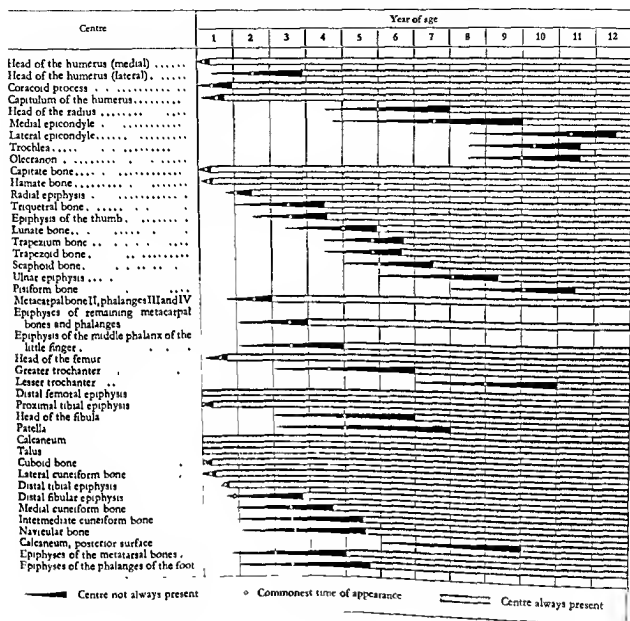
Bone age in the hand can be readily assessed by means of the table on page 708. For other bones and for a more detailed estimation of bone age see the special atlases¹⁻⁴.

In assessing bone development at and during puberty it must be remembered that girls have a bone age about two years in advance of that of boys of the same age.

Bone development and the onset of puberty

The onset of puberty can be predicted far more reliably from the state of bone development than from height, while chronological age is an even more unreliable guide. When bone development

Time of appearance of the ossification centres of the limb bones⁷



rapid and uninterrupted the onset of puberty will be early, and vice versa. In a similar way the time of appearance and state of development of the various ossification centres are directly related to the individual's eventual height. Thus from the age of 6 years

six months of the commencement of ossification of the apophysis of the iliac crest

Conditions in which it is important to determine bone age

Hypothyroidism—This is marked by a distinct delay in the appearance of the ossification centres. Serial determinations of bone age should accompany treatment. Excessively rapid skeletal development involves the danger of dwarfism.

Pituitary dwarfism—Bone age and longitudinal growth are delayed to the same extent.

Primordial dwarfism—Longitudinal growth is delayed but ossification remains practically normal for the child's age.

Pituitary gigantism—Again due to discordance, longitudinal growth being very advanced while ossification is normal for the child's age.

Adrenogenital syndrome—This is far in excess of the normal union.

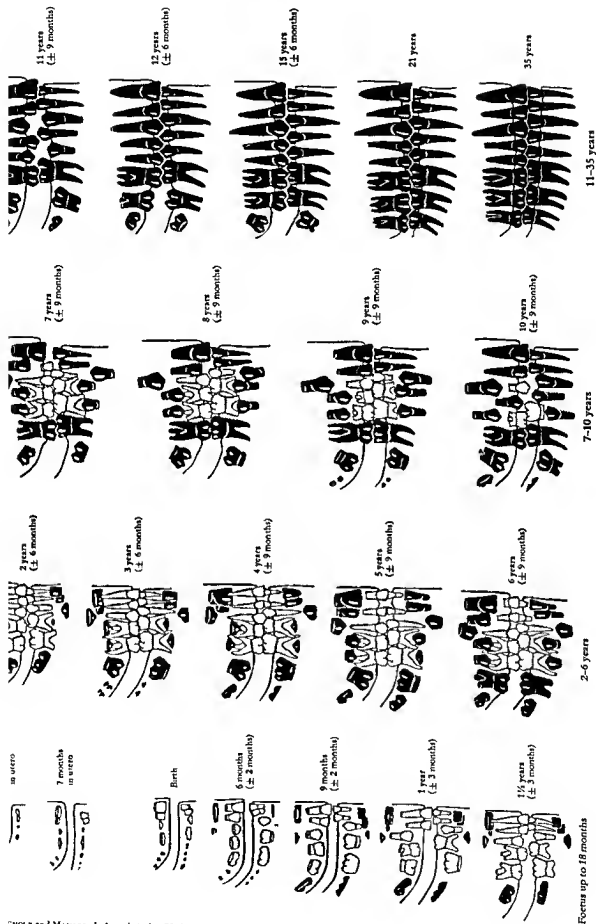
Pseudo—The longitudinal growth are abnormally rapid, the former more so than the latter.

References

Boys Number of individuals	Birth 116	6 months 92	1 year 101	1½ years 81	2 years 90	2½ years 78	3 years 78	3½ years 70	4 years 66	4½ years 53	5 years 52	5½ years 40	6 years 31	6½ years 19	P_{80}
															P_{80}
															P_{50} (mean)
															P_{10}
Girls Number of individuals	Birth 112	6 months 91	1 year 101	1½ years 80	2 years 86	2½ years 75	3 years 81	3½ years 67	4 years 61	4½ years 56	5 years 53	5½ years 41	6 years 32	6½ years 17	P_{80}
															P_{80}
															P_{50} (mean)
															P_{10}

80 % of all normal individuals

80 % of all normal individuals



Weights of the Organs

Organ weights at various ages (in grammes)¹

	Lungs		Brain		Heart		Kidneys		Liver		Spleen	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Newborn	51.7	50.9	353	347	19	20	24	24	124	125	8	-
0-3 months.....	68.8	63.6	435	411	-	-	-	-	-	-	-	-
3-6 months.....	94.1	93.3	600	534	-	-	-	-	-	-	-	-
6-9 months.....	128.5	114.7	877	726	41	36	60	52	300	240	26	2
9-12 months.....	142.4	142.1										
1-2 years.....	170.3	175.3	971	894	54	48	72	65	400	390	35	3
2-3 years.....	245.9	244.3	1076	1012	63	62	85	75	460	450	42	4
3-4 years.....	304.7	265.5	1179	1076	73	71	93	84	510	500	48	4
4-5 years.....	314.2	311.7	1290	1156	83	80	100	93	555	550	53	5
5-6 years.....	260.6	319.9	1275	1206	95	90	106	102	595	590	58	5
6-7 years.....	399.5	357.5	1313	1225	103	100	112	112	630	635	62	6
7-8 years.....	365.4	404.4	1338	1265	110	113	120	123	665	685	64	6
8-9 years.....	405.0	382.1	1294	1208	122	126	128	135	715	745	68	7
9-10 years.....	376.4	358.4	1360	1226	132	140	138	148	770	810	73	7
10-11 years.....	474.5	571.2	1378	1247	144	154	150	163	850	880	82	8
11-12 years.....	465.6	535.0	1348	1259	157	168	164	180	950	960	91	9
12-13 years.....	458.8	681.7	1383	1256	180	188	178	195	1050	1080	101	10
13-14 years.....	504.5	602.3	1382	1243	202	207	196	210	1150	1180	111	11
14-15 years.....	692.8	517.0	1356	1318	238	226	212	222	1240	1270	121	12
15-16 years.....	691.7	708.8	1407	1271	258	238	229	230	1315	1330	135	12
16-17 years.....	747.3	626.5	1419	1300	282	243	244	236	1380	1360	145	13
17-18 years.....	776.9	694.5	1409	1254	300	247	260	240	1450	1380	152	14
18-19 years.....	874.7	654.9	1426	1312	310	250	270	244	1510	1395	157	14
19-20 years.....	1035.6	785.2	1430	1294	318	251	282	247	1580	1405	160	15
20-21 years.....	953.0	792.8	-	-	322	252	290	248	1630	1415	162	15

Weights of endocrine organs (in grammes) (values are for both sexes)¹

	Adre-nals	Pitu-itary	Thy-mus	Pan-creas	Thy-roid		Adre-nals	Pitu-itary	Thy-mus	Pan-creas	Thy-roid
Newborn	9.04	-	10.9	2.77	2.09	2-4 years.....	-	-	-	19.44	-
2-14 days	5.19	-	-	-	-	2-5 years.....	4.71	0.194	-	-	-
0-1 month	-	-	-	2.42	-	3-5 years.....	-	-	28.0	-	-
1-2 months.....	-	-	-	2.63	-	4-6 years.....	-	-	-	22.44	5.24
0-3 months.....	-	-	-	-	1.71	6-8 years.....	-	-	-	28.46	7.05
2-3 months.....	-	-	-	4.46	-	5-10 years...	5.19	0.257	28.5	-	-
0-6 months.....	-	0.113	-	-	-	8-10 years.....	-	-	-	26.53	9.30
3-6 months.....	3.91	-	-	5.38	2.11	10-12 years.....	-	-	-	29.25	8.69
1 day to	-	-	-	-	-	12-14 years.....	-	-	-	-	14.82
12 months....	-	-	19.5	-	-	10-15 years..	7.00	0.380	29.5	-	-
6-12 months.....	4.73	0.127	-	9.24	2.04	14-16 years.....	-	-	-	-	14.48
1-2 years.....	3.56	0.148	-	13.54	2.53	16-18 years.....	-	-	-	-	16.62
1-3 years.....	-	-	23.0	-	-	15-20 years..	10.00	0.556	21.0	68.33	-
2-3 years.....	-	-	-	-	3.40	18-20 years.....	-	-	-	-	18.33
						20-25 years..	-	-	18.6	-	-

Weights of reproductive organs (in grammes)¹

	Testes	Testes and epididymides	Seminal vesicles	Prostate	Ovaries	Uterine tubes	Uterus
Newborn	0.85	0.91	0.050	0.82	0.33	0.29	3.90
0-1 year	1.03	1.33	0.052	0.9	0.62	0.26	1.42
1-2 years.....	-	-	-	-	0.84	0.29	1.50
1-3 years.....	1.48	1.82	-	1.2	-	-	-
2-4 years.....	-	-	-	-	1.12	-	2.30
3-5 years.....	1.64	1.76	-	1.1	-	-	2.80
4-7 years.....	-	-	-	-	1.90	-	-
5-10 years.....	1.67	2.24	0.099	1.3	-	-	-
10-12 years.....	2.00	4.00	0.120	1.9	-	-	-
7-14 years....	-	-	-	-	3.30	0.49	4.30
12-14 years.....	6.96	8.15	-	3.3	-	-	-
14-16 years.....	15.56	19.3	0.900	4.3	-	-	-
16-18 years.....	-	32.0	-	8.8	-	-	-
14-20 years..	-	-	-	-	6.03	1.05	32.50
20-30 years.....	34.66	-	-	16.6	10.71	2.13	49.50

Weights of the Organs

Organ weights at various ages (in grammes)†

	Lungs		Brain		Heart		Kidneys		Liver		Spleen	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	W
Newborn	51.7	50.9	353	347	19	20	24	24	124	125	8	
0-3 months.....	68.8	63.6	435	411	-	-	-	-	-	-	-	
3-6 months.....	94.1	93.3	600	534	-	-	-	-	-	-	-	
6-9 months.....	128.5	114.7										
9-12 months.....	142.4	142.1	877	726	41	36	60	52	300	240	26	
1-2 years.....	170.3	175.3	971	894	54	48	72	65	400	390	35	
2-3 years.....	245.9	244.3	1076	1012	63	62	85	75	460	450	42	
3-4 years.....	304.7	265.5	1179	1076	73	71	93	84	510	500	48	
4-5 years.....	314.2	311.7	1290	1156	83	80	100	93	555	550	53	
5-6 years.....	260.6	319.9	1275	1206	95	90	106	102	595	590	58	
6-7 years.....	399.5	357.5	1313	1225	103	100	112	112	630	635	62	
7-8 years.....	365.4	404.4	1338	1265	110	113	120	123	665	685	64	
8-9 years.....	405.0	382.1	1294	1208	122	126	128	135	715	745	68	
9-10 years.....	376.4	358.4	1360	1226	132	140	138	148	770	810	73	
10-11 years.....	474.5	571.2	1378	1247	144	154	150	163	850	880	82	
11-12 years.....	465.6	535.0	1348	1259	157	168	164	180	950	960	91	
12-13 years.....	458.8	681.7	1383	1256	180	188	178	195	1050	1080	101	10
13-14 years.....	504.5	602.3	1382	1243	202	207	196	210	1150	1180	111	11
14-15 years.....	692.8	517.0	1356	1318	238	226	212	222	1240	1270	121	12
15-16 years.....	691.7	708.8	1407	1271	258	238	229	230	1315	1330	135	12
16-17 years.....	747.3	626.5	1419	1300	282	243	244	236	1380	1360	145	13
17-18 years.....	776.9	694.5	1409	1254	300	247	260	240	1450	1380	152	14
18-19 years.....	874.7	654.9	1426	1312	310	250	270	244	1510	1395	157	14
19-20 years.....	1035.6	785.2	1430	1294	318	251	282	247	1580	1405	160	15
20-21 years.....	953.0	792.8	-	-	322	252	290	248	1630	1415	162	15

Weights of endocrine organs (in grammes) (values are for both sexes)†

	Adre-nals	Pitu-itary	Thy-mus	Pan-creas	Thy-roid		Adre-nals	Pitu-itary	Thy-mus	Pan-creas	Thy-roid
Newborn	9.04	-	10.9	2.77	2.09	2-4 years.....	-	-	-	19.44	-
2-14 days	5.19	-	-	-	-	2-5 years.....	4.71	0.194	-	-	-
0-1 month	-	-	-	2.42	-	3-5 years.....	-	-	28.0	-	-
1-2 months.....	-	-	-	2.63	-	4-6 years.....	-	-	-	22.44	5.2
0-3 months.....	-	-	-	-	1.71	6-8 years.....	-	-	-	28.46	7.0
2-3 months.....	-	-	-	4.46	-	5-10 years.....	5.19	0.257	28.5	-	-
0-6 months.....	-	0.113	-	-	-	8-10 years.....	-	-	-	26.53	9.3
3-6 months.....	3.91	-	-	5.38	2.11	10-12 years.....	-	-	-	29.25	8.6
1 day to 12 months...	-	-	19.5	-	-	12-14 years.....	-	-	-	-	14.8
6-12 months.....	4.73	0.127	-	9.24	2.04	10-15 years...	7.00	0.380	29.5	-	-
1-2 years.....	3.56	0.148	-	13.54	2.53	14-16 years.....	-	-	-	-	14.4
1-3 years.....	-	-	23.0	-	-	16-18 years.....	-	-	-	-	16.6
2-3 years.....	-	-	-	-	3.40	15-20 years...	10.00	0.556	21.0	68.33	-
						18-20 years.....	-	-	-	-	18.3
						20-25 years...	-	-	18.6	-	-

Weights of reproductive organs (in grammes)†

	Testes	Testes and epididymides	Seminal vesicles	Prostate	Ovaries	Uterine tubes	Uterus
Newborn	0.85	0.91	0.050	0.82	0.33	0.29	3.90
0-1 year	1.03	1.33	0.052	0.9	0.62	0.26	1.42
1-2 years.....	-	-	-	-	0.84	0.29	1.50
1-3 years.....	1.48	1.82	-	1.2	-	-	2.30
2-4 years.....	-	-	-	-	1.12	-	-
3-5 years.....	1.64	1.76	-	1.1	-	-	2.80
4-7 years.....	-	-	-	-	1.90	-	-
5-10 years.....	1.67	2.24	0.099	1.3	-	-	-
10-12 years.....	2.00	4.00	0.120	1.9	-	-	4.30
7-14 years...	-	-	-	-	3.30	0.49	-
12-14 years.....	6.96	8.15	-	3.3	-	-	-
14-16 years.....	15.56	19.3	0.900	4.3	-	-	-
16-18 years.....	-	32.0	-	8.8	-	-	-
14-20 years...	-	-	-	-	6.03	1.05	32.50
20-30 years.....	34.66	-	-	16.6	10.71	2.13	49.50

Height (in shoes)		Average weights in pounds and kilograms (in indoor clothing)															
		15-16 years		17-19 years		20-24 years		25-29 years		30-39 years		40-49 years		50-59 years		60-69 years	
		lb	kg	lb	kg	lb	kg	lb	kg	lb	kg	lb	kg	lb	kg	lb	kg
Men																	
0	152.4	98	44.5	113	51.3	122	55.3	128	58.1	131	59.4	134	60.8	136	61.7	133	60.3
0 1/2	153.7	100	45.4	114.5	51.9	123.5	56	129.5	58.7	132.5	60.1	135.5	61.5	137.5	62.4	134.5	61
1	154.9	102	46.3	116	52.6	125	56.7	131	59.4	134	60.8	137	62.1	139	63	136	61.7
1 1/2	156.2	104.5	47.4	117.5	53.3	126.5	57.4	132.5	60.1	135.5	61.5	138.5	62.8	140.5	63.7	137.5	62.4
2	157.5	107	48.5	119	54	128	58.1	134	60.8	137	62.1	140	63.5	142	64.4	139	63
2 1/2	158.8	109.5	49.7	121	54.9	130	59	136	61.7	139	63	142	64.4	143.5	65.1	140.5	63.7
3	160	112	50.8	123	55.8	132	59.9	138	62.6	141	64	144	65.3	145	65.8	142	64.4
3 1/2	161.3	114.5	51.9	125	56.7	134	60.8	139.5	63.3	143	64.9	146	66.2	147	66.7	144	65.3
4	162.6	117	53.1	127	57.6	136	61.7	141	64	145	65.8	148	67.1	149	67.6	146	66.2
4 1/2	163.8	119.5	54.2	129	58.5	137.5	62.4	142.5	64.6	147	66.7	150	68	151	68.5	148	67.1
5	165.1	122	55.3	131	59.4	139	63	144	65.3	149	67.6	152	68.9	153	69.4	150	68
5 1/2	166.4	124.5	56.5	133	60.3	140.5	63.7	146	66.2	151	68.5	154	69.9	155	70.3	152	68.9
6	167.6	127	57.6	135	61.2	142	64.4	148	67.1	153	69.4	156	70.8	157	71.2	154	69.9
6 1/2	168.9	129.5	58.7	137	62.1	143.5	65.1	149.5	67.8	155	70.3	158.5	71.9	159.5	72.3	156.5	71
7	170.2	132	59.9	139	63	145	65.8	151	68.5	157	71.2	161	73	162	73.5	159	72.1
7 1/2	171.5	134.5	61	141	64	147	66.7	153	69.4	159	72.1	163	73.9	164	74.4	161	73
8	172.7	137	62.1	143	64.9	149	67.6	155	70.3	161	73	165	74.8	166	75.3	163	73.9
8 1/2	174	139.5	63.3	145	65.8	151	68.5	157	71.2	163	73.9	167	75.8	168	76.2	165.5	75.1
9	175.3	142	64.4	147	66.7	153	69.4	159	72.1	165	74.8	169	76.7	170	77.1	168	76.2
9 1/2	176.5	144	65.3	149	67.6	155	70.3	161	73	167.5	76	171.5	77.8	172.5	78.2	170.5	77.3
10	177.8	146	66.2	151	68.5	157	71.2	163	73.9	170	77.1	174	78.9	175	79.4	173	78.5
10 1/2	179.1	148	67.1	153	69.4	159	72.1	165	74.8	172	78	176	79.8	177.5	80.5	175.5	79.6
11	180.3	150	68	155	70.3	161	73	167	75.8	174	78.9	178	80.8	180	81.6	178	80.8
11 1/2	181.6	152	68.9	157.5	71.4	163.5	74.2	169.5	76.9	176.5	80.1	180.5	81.9	182.5	82.8	180.5	81.9
12	182.9	154	69.9	160	72.6	166	75.3	172	78	179	81.2	183	83	185	83.9	183	83
0 1/2	184.2	156.5	71	162	73.5	168	76.2	174.5	79.2	181	82.1	185	83.9	187	84.8	185.5	84.1
1	185.4	159	72.1	164	74.4	170	77.1	177	80.3	183	83	187	84.8	189	85.7	188	85.3
1 1/2	186.7	161.5	73.3	166	75.3	172	78	179.5	81.4	185.5	84.1	189.5	86	191.5	86.9	190	86.4
2	188	164	74.4	168	76.2	174	78.9	182	82.6	188	85.3	192	87.1	194	88	193	87.5
2 1/2	189.2	166.5	75.5	170	77.1	176	79.8	184	83.5	190.5	86.4	194.5	88.2	196.5	89.1	195.5	88.7
3	190.5	169	76.7	172	78	178	80.8	186	84.4	193	87.5	197	89.4	199	90.3	198	89.8
3 1/2	191.8	-	-	174	78.9	179.5	81.4	188	85.3	196	88.9	200	90.7	202	91.6	201	91.2
4	193	-	-	176	79.8	181	82.1	190	86.2	199	90.3	203	92.1	205	93	204	92.5
Women																	
10	147.3	97	44	99	44.9	102	46.3	107	48.5	115	52.2	122	55.3	125	56.7	127	57.6
10 1/2	148.6	98.5	44.7	100.5	45.6	103.5	46.9	108.5	49.2	116	52.6	123	55.8	126	57.2	128	58.1
11	149.9	100	45.4	102	46.3	105	47.6	110	49.9	117	53.1	124	56.2	127	57.6	129	58.5
11 1/2	151.1	101.5	46	103.5	46.9	106.5	48.3	111.5	50.6	118.5	53.8	125.5	56.9	128.5	58.3	130	59
0	152.4	103	46.7	105	47.6	108	49	113	51.3	120	54.4	127	57.6	130	59	131	59.4
0 1/2	153.7	105	47.6	107	48.5	110	49.9	114.5	51.9	121.5	55.1	128.5	58.3	131.5	59.6	132.5	60.1
1	154.9	107	48.5	109	49.4	112	50.8	116	52.6	123	55.8	130	59	133	60.3	134	60.8
1 1/2	156.2	109	49.4	111	50.3	113.5	51.5	117.5	53.3	124.5	56.5	131.5	59.6	134.5	61	135.5	61.5
2	157.5	111	50.3	113	51.3	115	52.2	119	54	126	57.2	133	60.3	136	61.7	137	62.1
2 1/2	158.8	112.5	51	114.5	51.9	116.5	52.8	120.5	54.7	127.5	57.8	134.5	61	138	62.6	139	63
3	160	114	51.7	116	52.6	118	53.5	122	55.3	129	58.5	136	61.7	140	63.5	141	64
3 1/2	161.3	115.5	52.4	118	53.5	119.5	54.2	123.5	56	130.5	59.2	138	62.6	142	64.4	143	64.9
4	162.6	117	53.1	120	54.4	121	54.9	125	56.7	132	59.9	140	63.5	144	65.3	145	65.8
4 1/2	163.8	119	54	122	55.3	123	55.8	127	57.6	133.5	60.6	141.5	64.2	146	66.2	147	66.7
5	165.1	121	54.9	124	56.2	125	56.7	129	58.5	135	61.2	143	64.9	148	67.1	149	67.6
5 1/2	166.4	123	55.8	125.5	56.9	127	57.6	131	59.4	137	62.1	145	65.8	150	68	151	68.5
6	167.6	125	56.7	127	57.6	129	58.5	133	60.3	139	63	147	66.7	152	68.9	153	69.4
6 1/2	168.9	126.5	57.4	128.5	58.3	130.5	59.2	134.5	61	140.5	63.7	149	67.6	154	69.9	155	70.3
7	170.2	128	58.1	130	59	132	59.9	136	61.7	142	64.4	151	68.5	156	70.8	157	71.2
7 1/2	171.5	130	59	132	59.9	134	60.8	138	62.6	144	65.3	153	69.4	158	71.9	159	72.1
8	172.7	132	59.9	134	60.8	136	61.7	140	63	146	66.2	155	70.3	160	72.6	161	73
8 1/2	174	134	60.8	136	61.7	138	62.6	142	64.4	149	67.1	157	71.2	162	73.5	163	73.9
9	175.3	136	61.7	138	62.6	140	63.5	144	65.3	150	68	159	72.1	164	74.4	165	74.8
9 1/2	176.5	-	-	140	63.5	142	64.4	146	66.2	152	68.9	161.5	73.3	166.5	75.5	-	-
10	177.8	-	-	142	64.4	144	65.3	148	67.1	154	69.9	164	74.4	169	76.7	-	-
10 1/2	179.1	-	-	144.5	65.5	146.5	66.5	150.5	68.3	156.5	71	166.5	75.5	171.5	77.8	-	-
11	180.3	-	-	147	66.7	149	67.6	153	69.4	159	72.1	169	76.7	174	78.9	-	-
11 1/2	181.6	-	-	149.5	67.8	151.5	68.7	155.5	70.5	161.5	73.3	171.5	77.8	177	80.3	-	-
12	182.9	-	-	152	68.9	154	69.9	158	71.7	164	74.4	174	78.9	180	81.6	-	-

¹ Insured persons in the United States (Society of Actuaries, *Blood and Blood Pressure Study*, vol. 1, Chicago, 1959, page 16, with interpolations by the editors of this *Statistical Tables*). Compare the desirable weights in a similar population given in the table on page 712.

Desirable Weights of Adults¹

Height (in shoes)		Desirable weight in pounds and kilogrammes (in indoor clothing), ages 25 and over					
		Small frame		Medium frame		Large frame	
ft	in	cm	lb	kg	lb	kg	lb
Men							
5	2	157.5	112-120	50.8-54.4	118-129	53.5-58.5	126-141
5	3	160	115-123	52.2-55.8	121-133	54.9-60.3	129-144
5	4	162.6	118-126	53.5-57.2	124-136	56.2-61.7	132-148
5	5	165.1	121-129	54.9-58.5	127-139	57.6-63	135-152
5	6	167.6	124-133	56.2-60.3	130-143	59 -64.9	138-156
5	7	170.2	128-137	58.1-62.1	134-147	60.8-66.7	142-161
5	8	172.7	132-141	59.9-64	138-152	62.6-68.9	147-166
5	9	175.3	136-145	61.7-65.8	142-156	64.4-70.8	151-170
5	10	177.8	140-150	63.5-68	146-160	66.2-72.6	155-174
5	11	180.3	144-154	65.3-69.9	150-165	68 -74.8	159-179
6	0	182.9	148-158	67.1-71.7	154-170	69.9-77.1	164-184
6	1	185.4	152-162	68.9-73.5	158-175	71.7-79.4	168-189
6	2	188	156-167	70.8-75.7	162-180	73.5-81.6	173-194
6	3	190.5	160-171	72.6-77.6	167-185	75.7-83.5	178-199
6	4	193	164-175	74.4-79.4	172-190	78.1-86.2	182-204
Women							
4	10	147.3	92- 98	41.7-44.5	96-107	43.5-48.5	104-119
4	11	149.9	94-101	42.6-45.8	98-110	44.5-49.9	106-122
5	0	152.4	96-104	43.5-47.2	101-113	45.8-51.3	109-125
5	1	154.9	99-107	44.9-48.5	104-116	47.2-52.6	112-128
5	2	157.5	102-110	46.3-49.9	107-119	48.5-54	115-131
5	3	160	105-113	47.6-51.3	110-122	49.9-55.3	118-134
5	4	162.6	108-116	49 -52.6	113-126	51.3-57.2	121-138
5	5	165.1	111-119	50.3-54	116-130	49 -59	125-142
5	6	167.6	114-123	51.7-55.8	120-135	54.4-61.2	129-146
5	7	170.2	118-127	53.5-57.6	124-139	56.2-63	133-150
5	8	172.7	122-131	55.3-59.4	128-143	58.1-64.9	137-154
5	9	175.3	126-135	57.2-61.2	132-147	59.9-66.7	141-158
5	10	177.8	130-140	59 -63.5	136-151	61.7-68.5	145-163
5	11	180.3	134-144	60.8-65.3	140-155	63.5-70.3	149-168
6	0	182.9	138-148	62.6-67.1	144-159	65.3-72.1	153-173

¹ Weights of insured persons in the United States associated with lowest mortality (*Statist. Bull. Metrop. Life Insur. Co.*, 40, Nov.-Dec. 1959).

of particular enzymes¹.

P. (Ed.), *Mechanism of Hormone Action*, NATO Advanced Study Academic Press, New York, 1965

tropins of the anterior pituitary^{1,2}

stimulating hormone
luteal-ripening hormone)

ling hormone
(stimulating hormone = ICSH, corpus luteum-
hormone)

try

... .. of with a molecular weight

of various human gonadotropin preparations³

Origin	TSH preparations		
	Activity (IU/mg)	LH content (IU/mg)	Prepared by
tary	1000	< 10	BUTT
opausal urine	597	11	DONINI
	789	< 0.03	STEVENS
urine	59.5	24.2	DONINI
Origin	LH preparations		
	Activity (IU/mg)	FSH content (IU/mg)	Prepared by
tary	7500	< 1	HARTREE
opausal urine	447	18.9	DONINI
le urine	53.6	6.7	DONINI

... .. methods of assay

... .. following reference preparations are available⁴

International Reference Preparation of Human Menopausal Gonadotropin (IRP-HMG), known previously as HMG-24

... .. Reference Preparation of Human Menopausal

Human Pituitary Gonadotropin (NIH-HPL-Uh) of the National Institute of Health

S1).
Human Pituitary Gonadotropin: An International Reference Preparation is in course of development

Conversion factors for reference preparations (as mg or IU equivalent to 1 mg of 2nd IRP-HMG)^{4a}

Reference preparation	FSH ^a	LH ^a
2nd IRP-HMG	1	1
1st IRP-HMG	56	16
NIH-FSH-S1	0.31	-
NIH-LH-S1	-	0.0053
International Unit	8	8

^a Assayed by the ovarian augmentation method in rodents

^a Assayed by the rat ovarian ascorbic acid depletion method

There is a considerable literature on the assay and extraction of gonadotropins in body fluids^{5,7}. The following methods are in common use

Total gonadotropic activity: Increase in the weight of the uterus in

LH activity: Increase in ventral prostate weight in immature hypophysectomized rats^{7,8}; depletion of ovarian ascorbic acid¹² or cholesterol¹³ in pseudo-pregnant immature rats after intravenous

criteria of immunological methods for both hormones remain to be established

Biosynthesis, secretion, metabolism

have been detected in the urine of prepuberal children²⁶. In women, gonadotropin excretion shows characteristic fluctuations during the menstrual cycle with a maximum during the ovulatory phase shortly before the rise in basal temperature²⁷. LH is present in the urine in all phases of the cycle and like total gonadotropin excretion rises to a maximum at midcycle²⁸⁻³⁰. FSH is also found in the urine in all phases of the cycle but the excretion is not subject to any marked rhythmic change^{28,29}. After the menopause gonadotropin excretion is increased, with wide daily variations, as a result of the almost complete cessation of ovarian oestrogen secretion³¹. In male urine FSH and LH are present in about the same proportion as in menopausal urine²⁹.

Total gonadotropin excretion in urine

	Mean	Range	s	Reference
	mg 1st IRP-HMG/24 h			
Men, 18-40 years	7.7	3.8-18.1	-	47
Women, 18-35 years	4.9	2.7-7.1	-	47
Girls, 14-15 years.....	0.8	-	-	47
Girls, 10 years.....	0.3	-	-	47
Boy, 8 ½ years.....	0.5	-	-	47
	U 1st IRP-HMG/24 h			
Women, menstruating	9.0	3.0-15.7	-	48
Women, proliferation phase .	9.2	2.8-30.4	-	48
Women, ovulation phase ...	10.5	2.8-31.6	-	48
Women, luteal phase	7.4	2.9-14.9	-	48
Women, postmenopausal ...	76	35-158*	-	49
Men, 20-60 years	11	5-23*	-	50

* 95% range.

* 95% range.

Gonadotropin assay in urine enables primary gonadal insufficiency (increased excretion) to be distinguished from secondary gonadal insufficiency due to disturbance of pituitary function (decreased excretion).

The urine of both children and adults contains a gonadotropin-inhibiting factor, but the precise physiological significance of this substance is not known^{32,43}.

Regulation of gonadotropin secretion. Gonadotropin secretion is regulated by neurohumoral factors from the hypothalamus, the so-called 'gonadotropin-releasing factors' (GRF)³³. These reach the cells of the anterior lobe of the pituitary via the portal circulation of the gland³⁴. At present the best-known factor is LH-RF, a polypeptide of molecular weight between 1200 and 2500³⁵. When given to rats this factor causes a rise in the plasma LH level³⁶. Formation of LH-RF is inhibited by oestrogens and, at high dosage, by progesterone and testosterone³⁵. Direct inhibition of LH release through the action of oestrogens on the pituitary may also occur³⁷. Inhibition of FSH-RF formation appears to require larger amounts of oestrogens than that of LH-RF formation³⁸ and is also caused by testosterone³⁹. The regulation of gonadotropin secretion is subject to the influence of nervous impulses of central and peripheral origin^{40,41}. The interaction of the gonadal steroids with the hypothalamus and pituitary not only takes the form of a negative feedback mechanism but in some circumstances may result in stimulation of these glands (positive feedback)^{2,40}.

Biological activity

The gonadotropins act directly on the gonads of both sexes and indirectly on the male and female reproductive organs by stimulating the secretion of gonadal steroids. In both sexes FSH is responsible for maintaining gametogenesis, LH for stimulating the interstitial ovarian tissue, ovulation, corpus luteum formation and the production of androgens in the cells of LEYDIG. The interplay of the various regulatory mechanisms in the course of the menstrual cycle is still not fully understood. Together with LH, FSH induces growth of the follicle and secretion of oestrogens. Sudden release of LH results in ovulation and suppresses oestrogen secretion, but such a release can be inhibited by high blood levels of oestrogens and progestational substances; this is one reason for

their use in ovulation-inhibiting preparations. Administered FSH preparations from the human pituitary tissue following HCG has repeatedly been shown to induce ovulation⁴².

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	Amino-acid sequence*	ACTH activity (IU/mg)	
		in vitro†	in vivo†
α-ACTH (cattle).....	<div style="text-align: center;">NH₂</div> Ser-[A]-Asp-Gly-Glu-Ala-Glu-Asp-Ser-Ala-Glu-[B]-Phe 1 25 26 27 28 29 30 31 32 33 39	140	-
α-ACTH (sheep).....	<div style="text-align: center;">NH₂</div> Ser-[A]-Ala-Gly-Glu-Asp-Asp-Glu-Ala-Ser-Glu-[B]-Phe 1 25 26 27 28 29 30 31 32 33 39	177	100-150
α-ACTH (pig)..... (corticotropin A**, β-corticotropin)	<div style="text-align: center;">NH₂</div> Ser-[A]-Asp-Gly-Ala-Glu-Asp-Glu-Leu-Ala-Glu-[B]-Phe 1 25 26 27 28 29 30 31 32 33 39	90-150	80-150
α-ACTH (man).....	<div style="text-align: center;">NH₂</div> Ser-[A]-Asp-Ala-Gly-Glu-Asp-Glu-Ser-Ala-Glu-[B]-Phe 1 25 26 27 28 29 30 31 32 33 39	52	26
As α-ACTH (pig).....	As α-ACTH (pig)	-	115

Thyrotropin^{1,2}

(thyrotropic hormone, thyroid-stimulating hormone = TSH)

Chemistry³

Bovine and human thyrotropins are glycoproteins of molecular weight ca. 28000; in addition to amino acids the molecule contains glucosamine, galactosamine and mannose. A highly purified but unstable preparation from the human pituitary had an activity of 20 IU/mg². Bovine TSH is biologically active in all vertebrates but the activity varies with the species. A substance similar to TSH has been isolated from mammalian pituitaries and given the name heterothyrotropic factor (HTF)⁴; it has little TSH activity in but is highly active in fish.

1 Unit (IU) is equal to 13.5 mg of the 1st International Standard (see page 762). 1 IU = 1 USP Unit = ca. 10 JUNKMANN-Units (JSU).

of assay^{2,3,5}

TSH activity can be determined in vivo or in vitro by means of the histological or physiological effects on the thyroid. In vitro methods in common use are those of BAKKE et al.⁶ (weight change of thyroid slices) and of KIRKHAM⁷ and BOTTARI et al.⁸ (release of ¹³¹I from thyroid slices). In body fluids, TSH concentration can now also be measured by radioimmunoassay^{9,10}.

Biosynthesis, secretion, metabolism

TSH is formed in the basophilic β^1 -cells of the anterior pituitary¹¹. The rate of secretion is regulated by the concentration of thyroid hormone in the circulating blood through a negative feedback mechanism (see page 727), a rise in the blood level of free thyroxine depressing TSH secretion, a fall accelerating it. Regulation of TSH secretion involves a neurohumoral mechanism depending on the formation of a thyrotropin-releasing factor (TRF)¹². This neurohormone, probably a weakly basic polypeptide¹³, is secreted by the nuclei of the anterior hypothalamus and discharged into the portal arteries of the anterior pituitary, where it stimulates the release and possibly also the synthesis of TSH¹⁴. In adults the rate of secretion of TSH has been estimated at 50–225 μ g/24 h¹⁵, corresponding to a half-life for TSH of 39–68 min.

Serum TSH levels. There is disagreement over the absolute levels^{2,3}. Serum concentrations of less than 3 μ g/l have been measured by radioimmunoassay in 50 euthyroid subjects, 10 hypophysectomized subjects and 12 pregnant women³; in the same study the levels in patients with hypothyroidism were 3–100 times higher, in those with hyperthyroidism within the normal range. The serum level in children is the same as in adults^{16,26} but higher in the newborn²⁶ and old people¹⁶. The high plasma levels in hypothyroid patients are due to prolonged survival of TSH in the circulation and increased pituitary secretion of the hormone¹⁵.

Whether TSH is excreted in measurable amount in the urine is still uncertain.

Long-acting thyroid stimulator (= LATS; thyroid-stimulating globulin = TSG). This factor is probably involved in the pathogenesis of GRAVES' disease^{17,18}. In the bioassay of TSH its presence is revealed by the long duration of its stimulating action compared to TSH. LATS appears to be a γ G-globulin¹⁹; it is formed in the lymphatic system and has a half-life in the rat of 7 $\frac{1}{2}$ h¹⁷.

Exophthalmos is certainly not due to TSH and probably not to LATS; a possible cause is a substance secreted by the pituitary²⁰ (EPS = exophthalmos-producing substance).

Biological activity

TSH brings about both histological and metabolic changes in the thyroid. The former comprise a diminution in the colloid content and enlargement of the epithelial cells, while under long-continued TSH stimulation the vessels become more numerous and larger and the gland becomes hypertrophic. The metabolic changes appear within 5–30 min of administering TSH²¹ and include increased oxygen consumption, glucose oxidation, phospholipid turnover, RNA synthesis and sodium uptake as well as stimulation of the various steps in the formation and release of thyroid hormone, particularly the organic binding of iodine²², the formation of iodothyronines from iodothyrosines²³, the liberation of thyroid hormone from thyroglobulin²⁴, and the release of iodine from iodothyrosines²². The effects of LATS on the thyroid are similar to those of TSH but are delayed^{17,25}.

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Prolactin^{1,2}

(lactogenic hormone, luteotropin, mammatropin, prolactin hormone = PH, lutotropic hormone = LTH, lutcomammatropic hormone = LMTH)

Chemistry

Prolactin as isolated from the anterior pituitary of sheep, cattle and pigs is a polypeptide of molecular weight ca. 25000^{3,4}. The prolactin molecule from sheep and cattle contains 211 amino-acid residues arranged as a single chain³; that from pigs has a considerably higher cysteine content⁴.

Whether a primate prolactin exists is still uncertain⁵. Growth hormone from man and monkeys has been shown to have prolactin-like activity, and this activity is intrinsic to the growth hormone molecule. Other studies indicate that human growth hormone and prolactin are potentially separable⁶. A high prolactin activity but low growth hormone activity has been demonstrated in a human pituitary tumour²¹, thus providing further evidence that the two hormones are not identical.

Luteotropin, formerly thought to be a distinct hormone, is now regarded as identical with prolactin.

Units, methods of assay

1 International Unit (IU) is equal to 0.04545 mg of the 2nd International Standard (see page 762), obtained from the anterior pituitary of sheep.

Biological assay^{5,7,8}. Proliferation test on the pigeon crop⁹. Determination of mammatropic activity in rabbits¹⁰ or mice¹¹. Determination of luteotropic activity in rats¹² or mice¹³. Immunological methods have been devised¹⁴ but have not yet found clinical application.

Biosynthesis, secretion, metabolism²

Prolactin is formed in the acidophile cells (staining with acrocarmine or erythrosin) of the anterior pituitary. In mammals these cells exhibit increasing secretory activity during pregnancy and particularly lactation. Data on prolactin activity in the blood and urine of both men and women are to be found in the literature but in view of the difficulties of hormone extraction and determination they are of questionable reliability⁸.

Regulation of prolactin secretion². In contrast to its effect on the secretion of the other anterior pituitary hormones, the hypothal-

HGH is fairly stable, so that pituitaries removed at autopsy can be kept for months with little loss of activity if stored in acetone or at very low temperature. Hormone isolated by the usual methods is not homogeneous and can be separated into components, for example by gel filtration¹ into two and by electrophoresis² into three components.

The growth hormones from different species also differ (immuno-

19. The similar effect produced by large doses of progesterone and corticosteroids is probably an indirect one.

gical activity²

rats and mice, prolactin has a luteotropic effect similar to that of gonadotropins, while its mammatropic and lactogenic effects¹⁸

in mammals, prolactin plays an important part in the growth of mammary glands. In ovariectomized rats, administration of prolactin together with growth hormone results in complete involution of the mammary glands. In male animals, the

involution as a result of the suckling stimulus, so that lactation is maintained.

In male guinea-pigs and rats, prolactin has been reported to promote the growth of the prostate and seminal vesicles, but the biological role played by the hormone in the male animal²⁰ is obscure.

In man, prolactin from sheep has effects similar to those of growth hormone of human origin²⁰.

Growth hormone from various species²⁴

	Mol weight	No of amino acids	N terminal sequence	C terminal sequence	Isoelectric point
Sheep	47800	430	Phe and Ala	Thr Ala Phe	6.8
Ox	45000	416	Phe Ala-Thr and Ala Phe Ala	Cys Ala Phe	6.8
Pig	41600	-	Phe Pro Ala	Cys Ala Phe	6.3
Whale	39900	340	Phe Lys (?)	Leu Ala Phe	6.2
Monkey	25400	220	Phe-Thr (?)	Ala Gly Phe	5.5
Man	21500	188	Phe Pro Thr	Cys Gly Phe	4.9

Units, methods of assay²

Indirectly, growth hormone can be determined by means of the dose-dependent incorporation of tagged sulphur into the rib cage of hypophysectomized rats¹². This method measures the so-called sulphation factor, a component of human serum not identical with HGH but closely related to it.

Biosynthesis, secretion, metabolism

Growth hormone is very probably formed in the acidophilic α -

ORRIDGE and BELL, *Hormone Assays and Their Clinical Application*, 2nd ed., Livingstone, Edinburgh, 1966.

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The secretion of growth hormone is to some extent regulated by the hypothalamus, probably via the formation of a 'somatotropin-releasing factor'²⁶ which stimulates the pituitary. In rats it has been shown that exogenous growth hormone inhibits endogenous hormone secretion, indicating the existence of a feedback mechanism²⁷.

Plasma levels of growth hormone (ug/l)

	Mean	Range	s	Reference
Cord blood	49.7	—	57.8	36
Children under 12 months.	18.6	—	12.5	36
Children, 1-8 years	8.5	—	7.8	36
Children, 9-10 years	2.8	—	2.8	36
Adolescents, 11-17 years ..	14.0	—	13.4	36
Adults, hospitalized	0.55	—	0.68	36
Women, lactating	4.5	—	2.1	36
Women	4.91	0.9-10.6	3.32	37
Men	0.27	0.1-0.7	0.14	37

Physiological effects of growth hormone³⁵

Protein metabolism	Increased protein synthesis Nitrogen retention* Phosphorus retention* Potassium retention* Diminished urea excretion* Increased intracellular amino-acid transport Increased protein synthesis at ribosomes
Lipid metabolism	Intracellular lipolysis Increased free fatty acid level in plasma* Increased oxidation of fats* Increased ketogenesis in diabetics*
Carbohydrate metabolism	Exacerbation of diabetes* Reduced response to insulin* Diminished conversion of glucose into fat in fatty tissue
Mineral metabolism	Calcium metabolism Increased intestinal absorption* Increased urinary excretion* Sodium retention* Phosphorus retention* Increased blood-phosphate level* Increased serum alkaline phosphatase level*
Organs and tissues	Acromegaly Connective tissue Stimulation of chondroitin sulphate synthesis Stimulation of collagen synthesis Increased excretion of hydroxyproline* Increase in volume of interstitial fluid
* Demonstrable in man after administration of growth hormone.	

Biological activity

In man, as in other animal species, the body has a specific requirement for growth hormone. In 6-week-old rats hypophysectomy causes immediate cessation of growth, which recommences immediately when the hormone is administered and continues as long as the medication is continued. In children with pituitary hypofunction growth is often retarded in even the first year of life²⁸ and then slows down greatly in the subsequent years. Administration of HGH to individuals with dwarfism due to deficiency of this hormone causes them to grow normally or faster than normal²⁹, but animal growth hormone is inactive in this respect. One reason why hypopituitary dwarfism in some does not respond to doses of HGH is probably the formation of antibodies against the preparation used³⁰. For the therapeutic indications of growth hormone see the literature^{2,31}. Unlike and steroids, growth hormone causes no acceleration of the maturation of bone.

Growth hormone has many other effects on metabolism other than that on growth, as shown in the table on this page.

Growth hormone has an anabolic effect on protein metabolism with consequent decrease in urinary nitrogen excretion. The nitrogen retention may increase initially to 3-5 g³², whereas growing children, for instance, require only 0.2 g nitrogen per kg body weight. Protein synthesis is probably stimulated via the ribosomes, presumably through promotion of messenger-RNA synthesis³³. Insulin acts synergistically.

The modifications of lipid metabolism consist of a reduction in fat synthesis and mobilization of depot fat. The free fatty acid content of the blood increases.

Single doses of the hormone have an effect similar to that of insulin, namely a fall in the blood-sugar level. Over longer periods and at higher dosage, however, growth hormone reduces glucose tolerance and causes hyperglycaemia and ketosis (diabetogenic effect).

Changes in mineral metabolism due to growth hormone comprise retention of sodium, phosphorus, potassium and usually calcium. In the kidneys the rates of glomerular filtration, plasma flow and phosphate reabsorption are increased.

In cartilage, growth hormone stimulates the proliferation of chondrocytes, the incorporation of phosphate and the synthesis of collagen.

In experimental animals, human growth hormone has effects similar to those of prolactin.

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insulin⁸

HPL can be determined radioimmunologically in tissue extracts and body fluids⁸⁻⁹. The site of its production is the placenta¹⁰ and it is contained in the cytoplasm of the syncytiotrophoblast layer of this organ⁸. The hormone can already be detected in the blood and urine in the first trimester of pregnancy, with advancing gestation the plasma level rises and reaches a maximum at term⁸⁻⁹. The normal plasma level in the third trimester is $6.8 \pm 2.1 \text{ mg/lit}$. High levels have been measured in diabetic pregnant women, low levels

Melanotropin⁷

(melanocyte-stimulating hormone = MSH, melanophore hormone, chromatophore hormone, pigment hormone, intermedin)

Chemistry^{2,3}

Structure and biological activity of melanotropins²⁰

	Amino-acid sequence																			Activity (U/g)*		
ACTH	Ser	Tyr	Ser	Met	Glu	His	Phe	Arg	Trp	Gly	Lys	Pro	Val	Gly	Lys	Lys	Arg	Arg	Pro	**		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19			
α MSH (porcine, bovine, equine)	CH ₃ CO-	Ser	Tyr	Ser	Met	Glu	His	Phe	Arg	Trp	Gly	Lys	Pro	Val	NH ₂					1.0-2.0 $\times 10^{10}$		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18				
β MSH (porcine)	Asp	Glu	Gly	Pro	Tyr	Lys	Met	Glu	His	Phe	Arg	Trp	Gly	Ser	Pro	Pro	Lys	Asp		3.0-5.0 $\times 10^9$		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18				
γ MSH (bovine)	Asp	Ser	Gly	Pro	Tyr	Lys	Met	Glu	His	Phe	Arg	Trp	Gly	Ser	Pro	Pro	Lys	Asp		2.0 $\times 10^9$		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18				
δ MSH (equine)	Asp	Glu	Gly	Pro	Tyr	Lys	Met	Glu	His	Phe	Arg	Trp	Gly	Ser	Pro	Arg	Lys	Asp		1.2 $\times 10^9$		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18				
δ MSH (human)	Ala	Glu	Lys	Lys	Asp	Glu	Gly	Pro	Tyr	Arg	Met	Glu	His	Phe	Arg	Trp	Gly	Ser	Pro	Pro	Lys	Asp
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22

* Frog skin test in vitro.

** On a molar basis naturally occurring ACTH possesses about 1% of the activity of α -MSH, ACTH acetylated at the serine end about 10%.

^a Frog skin test in vitro.

^{**} On a molar basis naturally occurring ACTH possesses about 1% of the activity of α -MSH, ACTH acetylated at the serine end about 10%.

cluding that of human β -MSH²¹. The α -corticotropin-releasing factors (see page 725) have a structure very similar to that of α -MSH.

Units, methods of assay

Methods of assay depend on the ability of the hormone to cause dispersion of the pigment (mainly melanin) in the melanocytes of amphibian. The test object is the frog^{4,5} or, in vitro, its skin^{6,7}. The latter reacts to a concentration as low as 10^{-11} mol MSH per litre⁸. The activity of MSH preparations is usually expressed in units based on the test of SHIZUME et al.⁶, 1 unit being that amount with the same activity as 0.04 μ g of the standard preparation of these workers.

Biosynthesis and secretion

MSH is probably formed in the polygonal cells of the intermediate lobe of the pituitary, which derives from RATHKE's pouch, though it is also present in the anterior and posterior lobes. In view of the structural relationship of MSH to ACTH it is likely that the former is also synthesized in the same type of anterior pituitary cell as the latter⁹. Melanotropic activity has also been detected in plasma extracts, with particularly high values in pregnancy^{4,10}. In both tissue and plasma extracts it has been possible to separate melanotropic from corticotropic activity¹¹. Using a radioimmunological method, β -MSH concentrations of 20–90 ng/l have been found in human plasma¹². In frogs and rats there is evidence that MSH secretion is regulated by the blood level of MSH through a feedback mechanism; this mechanism probably causes the hypothalamus to release a factor inhibiting MSH secretion¹³. Melanotropic activity has also been found in urine; in women this varies during the course of the menstrual cycle and rises during pregnancy^{10,14}.

Biological activity

In cold-blooded animals MSH causes rapid expansion of the melanocytes and dispersion of the pigment (melanin) in these cells, with consequent darkening of the skin. This reversible, physiological process of pigment regulation enables the animal rapidly to adapt itself to the colour of its surroundings. In birds and mammals the pigment content of the melanocytes controls the intensity of skin coloration, a slow process known as morphological pigment regulation in which the role played by MSH is still obscure. Pigment dispersion in frogs takes place in the melanocytes of the epidermis and dermis; this effect is reversible, but only in the dermal melanocytes, by the pineal-gland factor melatonin¹⁵ (see page 730). Morphologically, the epidermal melanocytes of the frog are similar to those of mammals. MSH apparently increases pigment formation; thus the pigment content of frogs rises under long-term treatment with MSH, and in man daily injections of α -MSH result in hyperpigmentation already visible on the second day¹⁶. Other effects of administering MSH to mammals are hypocalcaemia, hyperlipaemia and increases in thyroid function, pulse rate and the permeability of the blood-aqueous barrier of the eye^{3,17}, but whether these actions occur at physiological levels of the hormone is not known.

The mode of action of MSH is still obscure. Melanin dispersion is probably only a secondary effect of some direct change in the cell involving sodium and calcium¹⁸. Melanin is formed in the melanocytes from tyrosine and oxygen (see page 440) in ribosomes containing *o*-diphenol oxidase, whereby these subcellular particles undergo a gradual 'melanization'. It is conceivable that MSH has some action on the enzyme *o*-diphenol oxidase, but this has not been demonstrated¹⁹.

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Oxytocin¹⁻³

(pitocin, lactagogen) (for references see page 725)

Vasopressin¹⁻²

(pitressin, antidiuretin, antidiuretic hormone = ADH)

Chemistry⁴

As isolated from the posterior pituitary of various species hormones oxytocin and vasopressin are cyclic polypeptides made up of 9 amino-acid residues, one disulphide bridge and one terminal amide group; the ring structure is formed from the disulphide form on oxidation of the cysteine residues⁵. The various oxytocin and vasopressins differ only in the nature of the amino acid positions 3, 4 and 8. The molecular weight is just over 1000. The structure and biological activity of the naturally occurring hormones are shown in the table on page 724. Arginine vasopressin occurs in most mammals whereas lysine vasopressin is confined to species of swine⁶. The aspartic acid residue in position 5 and glycineamide residue in position 9 are essential for oxytocin activity, while the basic side chain at position 8 is essential for diuretic activity⁶. The activity varies with the size of the ring; is not dependent on the existence of the disulphide bridge; activity persists after replacement of the cysteine S of position 1 by a C group⁷.

Units, methods of assay

Synthetic preparations of both these human posterior lobe hormones are available. 1 International Unit (IU) of oxytocic, vasopressor and antidiuretic activity is contained in 0.5 mg of the International Standard (see page 762).

Various biological methods are available for the assay of posterior lobe hormones⁸, some of which are given in the table on page 724. In interpreting the results it must be borne in mind that most tissues contain other pharmacologically active substances like histamine, serotonin, acetylcholine and bradykinin, to which the methods of bioassay used for the hormones also respond.

Assay of oxytocic activity is usually carried out by measuring the contractions produced by the preparation in the isolated uterus of rats pretreated with oestrogens (rat uterus test), that of vasopressor activity by determining the rise of blood pressure caused by the preparation in the carotid artery of rats. Radioimmunochemical techniques may soon be available⁹.

Biosynthesis, secretion, metabolism¹⁰

Oxytocin and vasopressin are formed in the hypothalamus and stored in the posterior lobe of the pituitary. The Golgi apparatus of the hypothalamic neurones, the nucleus supraopticus and nucleus paraventricularis produce a neurosecretory protein material that is deposited as required in nerve endings in the posterior lobe, a process requiring its transport by the axoplasm of the supraopticohypophyseal tract¹¹. Both oxytocin and vasopressin have been isolated from this material. The neurosecretion can be demonstrated under the optical microscope by suitable staining (for example GOMORI's); under the electron microscope it appears as dense granules 0.1–0.3 μ m in diameter. The accumulation of the granules accounts for the specific staining of the nerve endings as for HERRING's bodies. When the pituitary stalk is cut the neurosecretion accumulates in the proximal ends of the axons. Physiological stimuli depleting neurohypophyseal activity also deplete stainable neurosecretion in the hypothalamus and posterior pituitary.

* If the cysteine residues linked by the disulphide bridge are reckoned as a single amino acid (cysteine) oxytocin and vasopressin are octapeptides.

(For references see page 725)

and bladder in tailless amphibians - but increasing their permeability

polarization following electrical or chemical stimulation². At the biomolecular level the change in permeability is possibly due to enhanced synthesis of cyclic adenosine 3',5'-phosphate²⁴. Vasopressin-like polypeptides (see page 725) and possibly also vaso-individual secretory neurons secreting only one hormone and species differences in the proportion of vasopressin-producing oxytocin-producing neurons in the nuclei supraopticus and ventricularis¹⁴.The neurosecretory cells with thickened nerve endings contain secretion attach themselves to the walls of the posterior lobules and there give up their hormones; this process is calcium-dependent¹⁸.The posterior lobe was formerly thought always to release oxytocin and vasopressin together into the circulating blood, regardless of the nature of the stimulus. Several examples of independent release have, however, been described^{17, 19, 20}. Thus vasopressin, not oxytocin, is secreted following haemorrhage and on stimulation of the sinus nerve by carotid occlusion, while oxytocin, but

severe injury to the hypothalamus or destruction of the neurosecretory cells.

The effect of oxytocin on milk ejection is so powerful that injection of as little as 0.01 IU has an action on the mammary glands of lactating women²¹. Release of oxytocin from the posterior pituitary is initiated by the suckling stimulus, but there may be considerable psychic modifications of this reflex activity.The physiological function of vasopressin consists of a role in the production of hypertonic urine²². When the hormone is absent from the blood the aqueous permeability of the distal convoluted and collecting tubule of the nephron is lowered. In water diuresis the hypotonic fluid flowing out of the ascending part of the loop of Henle into the distal convoluted tubule remains hypotonic up to the mouth of the collecting tubule. Absorption of water in these parts of the tubule almost ceases since the reduced aqueous permeability means that there is no osmotic transfer of water to the isotonic interstice of the cortex and hypertonic interstice of the medulla. In the presence of vasopressin, on the other hand, the aqueous permeability of the distal convoluted tubule and collecting tubule is increased so that water can be pumped against an osmotic gradient, and active transport of water in this way has so far never been observed, in the production of both hyper- and hypotonic urine only solute particles (mainly sodium ions) are actively transported, the subsequent osmotic transfer of water being prevented by the impermeability of the

to be pumped against an osmotic gradient, and active transport of water in this way has so far never been observed, in the production of both hyper- and hypotonic urine only solute particles (mainly sodium ions) are actively transported, the subsequent osmotic transfer of water being prevented by the impermeability of the

The release of vasopressin from the posterior pituitary is thought to be regulated by the total osmotic concentration of electrolytes in the extracellular fluid. Thus when loss of water by the body causes the osmotic concentration to rise, more antidiuretic hormone is released, more water is reabsorbed in the kidneys, and a more concentrated urine is produced. Excessive intake of water has the opposite effect and a very dilute urine is produced (water diuresis). However, the osmotic concentration undergoes only slight

used in these media by the methods at present available. The plasma vasopressin level at a normal state of hydration has been estimated at 1-5 mIU/l (1 mIU = 1×10^{-11} mol) (for measured values see the table below).Vasopressins are found only in the plasma and are not bound to the erythrocytes²³. It is uncertain to what extent the hormones are bound to plasma proteins; under physiological conditions they are probably mainly present in the free form¹⁸.

Vasopressin contents of the peripheral plasma (mIU/l)

Normally hydrated		Dehydrated		Reference
Mean	Range	Mean	Range	
1.5	1.0-2.7	6.5	3.4-9.0	26
0.0	-	4.6	2.5-10.0	27
-	0.2-0.4	-	0.9-1.0	28

The hormones disappear rapidly from the plasma. The half-life of oxytocin in plasma is about 1-2 min, while that of vasopressin is about 5-10 min. The hormones are also found in other tissues such as the mammary glands, the myometrium in pregnancy and the placenta. In pregnant women the enzyme oxytocinase appears in the serum and is capable of breaking down both hormones.

A syndrome of hyponatraemia has been recognized in which the plasma vasopressin level has been found to be elevated. This syndrome is known as the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Biological activity

The posterior pituitary hormones act on the epithelial cells of the distal renal tubules in mammals and the analogous

	Structure	Oxytocin-like activity (IU/mg)				Vasopressin-like activity (IU/mg)		Occurrence
		Uterus (rat, in vitro)	Blood pressure (chicken)	Mammary glands (rabbit)	Blood pressure (rat)	Anti-diuresis (rat)		
Arginine vasopressin..... (Arg ⁸ -vasopressin)	Cys-Tyr-Phe-Glu(NH ₂)-Asp(NH ₂)-Cys-Pro-Arg-Gly-NH ₂ 1 2 3 4 5 6 7 8 9	16	60	70	400	400	Man, many mammals	
Lysine vasopressin (Lys ⁸ -vasopressin)	Cys-Tyr-Phe-Glu(NH ₂)-Asp(NH ₂)-Cys-Pro-Lys-Gly-NH ₂ 1 2 3 4 5 6 7 8 9	5	40	45	280	250	Pig, hippopotamus	
Oxytocin (Ile ³ -Leu ⁸ -vasopressin)	Cys-Tyr-Ile-Glu(NH ₂)-Asp(NH ₂)-Cys-Pro-Leu-Gly-NH ₂ 1 2 3 4 5 6 7 8 9	450	450	450	5	5	Man, many vertebrates	
Arginine vasotocin (Ile ³ -Arg ⁸ -vasopressin)	Cys-Tyr-Ile-Glu(NH ₂)-Asp(NH ₂)-Cys-Pro-Arg-Gly-NH ₂ 1 2 3 4 5 6 7 8 9	155	285	210	245	250	Birds, reptiles, fish	
Isotocin (Ser ¹ -Ile ³ -oxytocin, Ile ³ -Ser ¹ -Ile ⁸ -vasopressin)	Cys-Tyr-Ile-Ser-Asp(NH ₂)-Cys-Pro-Ile-Gly-NH ₂ 1 2 3 4 5 6 7 8 9	150	320	300	0.06	0.18	Many bony fish	
Mesotocin (Ile ³ -Ile ⁸ -vasopressin)	Cys-Tyr-Ile-Glu(NH ₂)-Asp(NH ₂)-Cys-Pro-Ile-Gly-NH ₂ 1 2 3 4 5 6 7 8 9	289	498	328	6	1.1	Frog, bichir	
Glumitocin..... (Ile ³ -Ser ¹ -Glu ⁸ -vasopressin)	Cys-Tyr-Ile-Ser-Asp(NH ₂)-Cys-Pro-Glu(NH ₂)-Gly-NH ₂ 1 2 3 4 5 6 7 8 9	8					Many elasmobranch fish	

the median eminence of the pituitary stalk. Factors identified in the hypothalamus (or neurohypophysis) of various animal species are listed in the table below.

Hypothalamic pituitary-regulating factors

	Abbreviation	Reference
Corticotropin-releasing factors	α_1 -CRF	5
	α_2 -CRF	6
	β -CRF	6,7
Melanocyte-stimulating-hormone releasing factor	MRF (MSH-RF)	8
Melanocyte-stimulating-hormone inhibiting factor	MIF (MSH-IF)	9
Follicle-stimulating-hormone releasing factor	FRF (FSH-RF)	10
Luteinizing-hormone releasing factor	LRF (LH-RF)	11
Prolactin-releasing factor	PRF (pigeons)	12
Prolactin-inhibiting factor	PIF (mammals)	13
Growth-hormone releasing factor	GRF (GH-RF)	14
Thyroid-stimulating-hormone releasing factor	TRF (TSH-RF)	15

SO THAT THIS hormone does not appear to be a simple polypeptide

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Thyroid hormones¹⁻³ (for references see page 728)

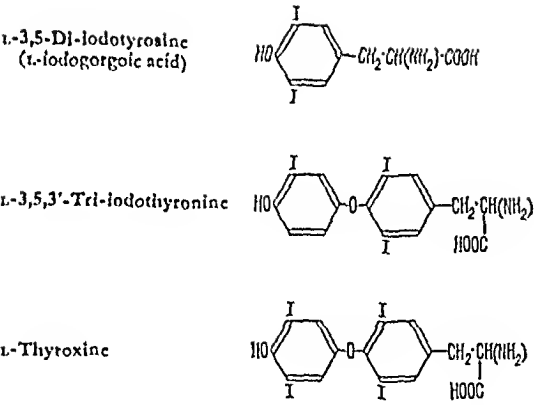
Chemistry

The normal human thyroid gland contains about 8 mg of iodine.⁴ Over 99% of this iodine is present in the organic form as the iodinated amino acids moniodotyrosine, diiodotyrosine, triiodo-thyronine and thyroxine



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(For references see page 728)



thyroid. Iodide concentration also occurs in other organs, su the salivary glands, gastric mucosa, skin, mammary glands placenta, but only in the thyroid is this process subject to ph logical regulation. Iodide concentration by the thyroid is st lated by thyrotropin, inhibited by hypophysectomy. The iodi oxidized to iodine or iodinium ions in the epithelial cells of thyroid follicles under the action of the enzyme peroxidase. still not clear whether iodination of the amino acids and coug of the tyrosines to thyronines takes place in the cells of the thy at the cell-colloid boundary, or even in the colloid itself. known, however, that there are variations in the degree of iod tion as well as in the structure of the thyroglobulin in the foll lar lumina.

The thyroid hormones – thyroxine and tri-iodothyronine – discharged into the blood only after enzymatic breakdown of thyroglobulin, a process stimulated by thyrotropin. Thyroglob is also present in the lymph of the thyroid, but the physiolog significance of the transport of this substance by the lymph system is unknown⁷. The mono- and di-iodotyrosines arising fr the breakdown of thyroglobulin are deiodinated in the thyroid, iodine so liberated being again available for the synthesis of thyr hormones.

Over 90% of the circulating thyroid hormones consists of ti roxine. Mono- and di-iodotyrosines do not appear to be norm: present in the blood⁸, although there are reports to the contrar. Most of the thyroxine in the serum is bound physicochemically certain carrier proteins⁹, the tri-iodothyronine to a much smal extent (for normal values of the protein-bound iodine see page 5 and the lower table below). Thyroxine is mainly linked to 'thy rene-binding globulin', lying electrophoretically between the α_1 - and α_2 -globulins, and 'thyroxine-binding prealbumin', though some present in the albumin fraction. Dialysis against a protein-free buff shows that the proportion of the total thyroxine present in the fr state is about 0.05%; the proportion of free tri-iodothyronine some 10 times greater¹¹. Very probably only the free thyroid ho

In the thyroid by far the greater part of these iodinated amino acids is bound to high-molecular proteins, the most important of which is thyroglobulin, a glycoprotein with a molecular weight of 660 000 and a sedimentation constant of 19 S⁵. Each molecule of thyroglobulin contains roughly 110 tyrosine residues and 26 atoms of iodine⁶; it has also been estimated that each molecule includes 7 monoiodotyrosine residues, 6 di-iodotyrosine residues and 1 thyroxine residue, while every third molecule contains a tri-iodothyronine residue. The proportions of the individual iodinated amino acids present in thyroglobulin depend on the iodine uptake; thus iodine deficiency results in an increase in the proportion of mono-iodotyrosine and tri-iodothyronine.

Biosynthesis, secretion, metabolism

The iodine ingested with food is transported by the blood in the form of iodide, which is then taken up in large amounts by the

Metabolic data for iodide*³

Age (years)	Plasma iodide concentration (µg/l)				Iodide clearance by thyroid (ml/min)				Absolute iodine uptake of thyroid (µg/h)				Renal iodide clearance (ml/min)			
	Men		Women		Men		Women		Men		Women		Men		Women	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
0-19 ..	1.4	~	0.8	0.6-1.0	23.0	~	36.2	31.5-40.9	2.0	~	1.6	1.4-1.9	27.0	~	31.5	30.2-32.7
20-39 ..	2.3	0.8-3.4	1.6	0.4-2.7	27.5	9.7-57.8	26.4	19.7-38.2	3.2	1.9-8.2	2.2	0.9-3.4	40.6	25.9-61.8	25.0	15.7-41.3
40-59 ..	1.7	0.4-3.6	1.6	0.8-2.6	21.8	2.9-38.5	15.6	5.7-37.6	2.5	0.1-6.7	1.3	0.6-2.2	38.8	17.9-53.8	28.4	19.0-37.4
> 60 ..	1.7	0.4-3.5	2.5	1.4-5.7	25.3	13.8-36.0	18.3	5.4-38.6	2.0	0.8-2.9	2.1	0.5-3.1	27.2	21.0-30.8	19.3	11.7-38.5

* Wide deviations from these values may occur in subjects with a high iodine intake.

Thyroid hormones in blood³⁵

Age (years)	Endogenous thyroxine distribution (%)						Thyroxine-binding capacity (µg thyroxine/l serum)				Protein-bound iodine (µg/l serum)		Free thyroxine			
	Thyroxine-binding globulin		Thyroxine-binding prealbumin		Albumin		Thyroxine-binding globulin		Thyroxine-binding prealbumin		Mean		(ng/l serum)		(% of total serum thyroxine)	
	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s	Mean	s
2-12 ..	55.0	7.0	26.8	5.5	18.2	3.7	27.3	3.6	72	26	61	7	47.0	7.4	0.050	0.007
16-20 ..	43.4	7.2	39.6	6.5	17.0	3.9	-	-	-	-	52	7	36.0	7.7	0.050	0.015
21-30 ..	40.2	4.0	43.1	5.9	16.6	3.3	-	-	-	-	52	11	44.6	14.1	0.057	0.015
31-40 ..	39.5	5.7	44.6	5.8	15.8	1.5	21.5	3.6	183	26	52	7	42.7	9.1	0.055	0.011
41-50 ..	41.7	7.1	42.7	7.9	15.7	2.5	-	-	-	-	53	9	46.0	11.4	0.057	0.008
51-60 ..	44.6	6.3	37.8	6.4	17.7	4.3	-	-	-	-	48	5	35.1	3.8	0.050	0.004
61-70 ..	47.8	9.7	36.5	8.9	15.5	3.1	25.3	5.8	128	60	54	8	47.5	12.3	0.058	0.014
> 70 ..	50.8	4.7	29.7	5.8	19.5	7.3	-	-	-	-	51	12	42.0	13.4	0.054	0.008

- **dris, alteration of the permeability of the mitochondrial membrane, and stimulation of protein synthesis. Some workers regard the last-named action as a primary effect of the hormones to which the calorigenic action is secondary.**

so The effects of the thyroid hormones and related compounds are closely linked with their chemical structure²⁷. In the iodinated thyronines the atelic configuration appears to be mainly responsible for biological activity, so that the presence of two iodine

enterally tri-iodothyronine is twice as active as thyroxine, when given orally four times as active. While thyroxine and tri-iodothyronine have qualitatively the same effects the calorigenic action of the latter is considerably quicker but not so long-lasting

Evaluation of thyroid function^{2,28}

Little can be deduced as to the functional state of the thyroid from its size and shape alone. Except in hyperthyroidism, hyperplasia of the gland merely reflects its increased stimulation by thyrotropin due to increased secretion of this hormone triggered by a reduction in the concentration of thyroxine in the blood (feedback mechanism). This reduction is in turn the result of a substrate

cept in the presence of extreme iodine deficiency or severely impaired synthesis. A severe functional disturbance may, however, be unaccompanied by goitre.

The functional state of the thyroid is best assessed by studying the individual phases of the iodine cycle: iodine uptake, hormone synthesis, hormone release, hormone transport, peripheral hormone uptake, iodine excretion. There is an equilibrium between these various phases that is also maintained in both hypo- and hyperthyroidism. In hyperfunctioning of the thyroid the iodine uptake of the gland is increased along with the rate of hormone synthesis, and the circulating free thyroid hormones are more quickly taken up by the tissues and broken down. In hypofunctioning of the gland all these phases are slowed down. The apparent thyroid hyperfunctioning of pregnancy is the result of increased renal iodine clearance with a compensating increase in thyroid function²⁹.

Iodine uptake phase Measurement of the accumulation of a radioactive iodine isotope first as I¹³¹ or I¹²⁵ in the thyroid gland is a

the important property of stimulating the maturation of cerebral cortex in the critical phase of development²⁵

relative potencies of the thyroid hormones and related compounds^{12, 29}

	Species	Physiological test		
		Calorigenic action	Growth and differentiation	Thyrotropin depression
thyroxine	All	100	100	100
thyroxine	Rat	5-8	-	-
	Man	8-12	-	-
3'-Tri-iodo-L-thyronine	Rat	150-350	500	-
	Man	100-250	-	280-540
3'-Tri-iodo-D-thyronine	Rat	10-15	-	14
3,5-Di-iodo-L-thyronine	Rat	0-5	-	-
3,5-Di-iodo-L-thyronine	Rat	0-3	-	-
3,5-Di-iodo-3'-methyl-DL-thyronine	Rat	150	-	-

the action of the thyroid hormones is marked by a so-called 'on period', thus in man the basal metabolic rate only begins to rise 2 days after their administration.

The bimolecular effects of the thyroid hormones have also been studied²⁶. These include modification of the activity of many enzymes, uncoupling of oxidative phosphorylation in the mitochondria.

Hormone uptake phase Measurement of the half-life of intravenously injected radioactive thyroxine (see p. 728).

Thyroid activity can also be evaluated indirectly from the activity of the thyroid hormones, for example by measuring the BMR (see page 539), the oxygen consumption of the leucocytes, or the time of the Achilles tendon reflex³⁴ (slowed in thyroxine deficiency, accelerated in thyroxine excess).

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Parathyroid hormone¹⁻³ (parathormone)

Chemistry

Purified bovine parathyroid hormone has a molecular weight of 8500 and is a single-chain polypeptide with no covalent intra-chain cross linkage⁴. A highly purified preparation with a biological activity of 2500-3000 USP units per milligramme can be obtained by gel filtration. The empirical amino-acid composition of bovine parathyroid hormone is Lys, His, Arg, Asp, Thr, Ser, Glu, Pro, Gly, Ala, Val, Met, Ile, Leu, Tyr, Phe, Trp. Parathyroid hormone is inactivated irreversibly by pepsin, trypsin and chymotrypsin, reversibly by hydrogen peroxide.

Units, methods of assay⁵

1 USP Unit = $\frac{1}{100}$ of the amount that when administered parenterally to dogs weighing 8-16 kg increases the serum calcium concentration by 1 mg/100 ml within 16-18 hours. The activity of

preparations can be determined by making use of this action on serum calcium level⁶ or by measuring their effect on the urinary phosphate excretion of parathyroidectomized rats⁷. The amount of the hormone present in body fluids can be determined by measuring its immunological properties, using either the complement-fixation test⁸ or radioimmunological methods⁹.

Biosynthesis, secretion, metabolism

Parathyroid hormone is formed in the chief cells, the light cells and possibly also the oxyphile cells of the parathyroid¹⁰. Intracytoplasmic droplets seen in GOLGI's apparatus may represent an intracellular form of the hormone¹¹. Discharge of the hormone into the blood is regulated by the diminution in the concentration of ionized calcium in the blood flowing into the parathyroid. This does not apply in primary hyperparathyroidism, in which the parathyroid secretes the hormone independently of the blood calcium level. The hypothalamus and pituitary have no detectable effect on the secretion of parathyroid hormone. A substance immunologically similar to parathyroid hormone is produced by nonendocrine tumours¹².

Published data on the parathyroid hormone content of the blood vary widely. Biological methods give values of 25 $\mu\text{g/l}$ plasma or more, radioimmunoassay values of 0.1 to 1.0 $\mu\text{g/l}$ plasma. The plasma level is increased in adenoma of the parathyroid, some form of carcinoma (pseudohyperparathyroidism) and chronic kidney disease (secondary hyperparathyroidism)¹³. The circulating hormone is rapidly broken down (half-life in rats 22 min¹⁴), probably in the liver. Parathyroid hormone is excreted in the urine, the amount decreasing as the level of ionized calcium in the serum rises¹⁵.

Biological activity

Parathyroid hormone maintains the concentration of ionized calcium in the extracellular fluid, a function in which vitamin D (see page 461) and thyrocalcitonin (see page 718) are also involved. The hormone has a direct action on bone¹⁶, in which it causes breakdown of the bone substance reflected in an increase not only of the blood calcium but also of the urinary excretion of mucopolysaccharides¹⁷, hydroxyproline¹⁸ and pyrophosphate¹⁹.

The other site of action of parathyroid hormone is the renal tubules, where it promotes the excretion of inorganic phosphate 15-40 min after administration of the hormone the latter reaches maximum lasting several hours, and the consequent fall in the serum phosphate level entails a rapid rise in the serum calcium level. Mobilization of calcium takes place more slowly, however, with a maximum after 6 hours or more, since it is preceded by an increased formation of osteoclasts²⁰. There are also indications that the hormone maintains the blood calcium level by stimulating tubular reabsorption of calcium²¹ and intestinal calcium absorption²². Parathyroid hormone has also been observed to have an effect on lactation²³.

The mode of action of parathyroid hormone has been extensively investigated. The hormone could act on the skeleton by (a) releasing a collagenolytic factor from the bone cells²⁴, and (b) promoting the formation of citrate and lactate and thus displacing it to the acid side, with a consequent increase in dissolution of the hydroxyapatite of bone²⁵. The action of the hormone on bone, but not that on renal tubular function, requires the presence of vitamin D^{26,27}. At the molecular level parathyroid hormone increases the uptake of phosphate by the mitochondria and, in conjunction with vitamin D, the mobilization of calcium^{28,29}. The action on bone is inhibited by actinomycin D, so that this effect, unlike that on the renal tubules, probably has a genetic mechanism^{11,29}.

Evaluation of parathyroid function^{30,31}

Hyperparathyroidism is often accompanied by a rise in serum calcium, increased urinary excretion of phosphate and calcium, and a fall in serum phosphate. The urinary phosphate excretion can be measured by the phosphate clearance³², by the percentage tubular reabsorption of phosphate³³, or by the phosphate excretion in dex³⁴ (see also page 663). Parathyroid suppression tests have been developed for distinguishing primary hyperparathyroidism from other diseases accompanied by disturbance of calcium metabolism^{31,35}; these involve measurement of the effect of a calcium infusion on phosphate excretion.

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Thymus hormone

In adult healthy mice thymectomy has virtually no effect except for slight lymphopenia, whereas in newborn animals the operation results in very severe disturbances all of which have their origin in state of immunological insufficiency¹. Intraperitoneal reimplantation of the thymus in a diffusion capsule is followed by reversal of these changes to a very large extent. It has been concluded that the thymus produces a humoral factor involved in the development of immunological competence (competence-inducing factor), possibly by furthering the maturation or differentiation of immunologically competent cells from their lymphoid precursors². The formation by the thymus of a humoral factor stimulating the proliferation of lymphatic tissue (lymphocyte-stimulating factor) had been postulated earlier³. Such a factor is possibly produced by the medullary epithelioid cells of the thymus in the form of an acid mucopolysaccharide containing sulphate⁴. A lymphopoietic factor active in vitro has been isolated from calf thymus and identified as heat-stable protein containing carbohydrate⁵. The immunological reactivity of thymectomized mice can be restored by administering an extract of calf thymus⁶. Several humoral factors may contribute to the functioning of the thymus⁷.

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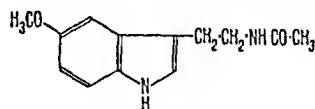
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Hormones of the pineal gland

In man the pineal organ is a conical, midline structure about 5 mm long located on the dorsal posterior edge of the epithalamus. It arises embryologically as an evagination of the neuroectoderm of the dorsal diencephalon. It is composed of epithelioid parenchymal cells, and usually contains calcareous deposits in sexually mature individuals. Phylogenetically it is the remnant of midline dorsal light receptors.

Possible pineal hormones. Melatonin (melanocyte-contracting principle, skin-lightening factor) is produced in the vertebrate pineal¹. Melatonin, as well as its metabolites such as 5-hydroxyindoleacetic acid, occur in the mammalian pineal in high concentrations. Noradrenaline and histamine are found in pineal extracts². Anoestrin, an inhibitor of oestrus, and antigonadotrophic factors have also been alleged to be present in the pineal; they may be identical with melatonin³. Glomerulotropin (adrenoglomerulotropin), an accelerator of aldosterone secretion, has been postulated as a pineal hormone⁴; it is reported to be a carboline derivative⁵.

Melatonin (N-acetyl-5-methoxytryptamine)



Melatonin is formed in the pineal gland by methylation of 5-acetyl-5-hydroxytryptamine¹, the reaction being catalysed by 5-hydroxyindole O-methyltransferase, a specific enzyme apparently occurring only in the mammalian pineal². The circulating melatonin is rapidly taken up by the tissues, where it is converted mainly into 6-hydroxymelatonin; this substance is excreted in the urine mainly as the sulphate and to a smaller extent as the glucuronate³.

In rats, the weight, morphology and chemical composition of the pineal gland can be altered by exposing the animals for long periods to continuous light or darkness. Thus light exposure causes the parenchymal cells to contract⁴, while dark exposure increases the activity of the enzyme hydroxyindole O-methyltransferase and therefore the rate of melatonin synthesis⁵. The serotonin, melatonin and hydroxyindole O-methyltransferase contents of the pineal gland are subject to a day-and-night rhythm^{6,7} as a result of sympathetic nervous regulation by the amount of light entering the eyes.

In amphibia, melatonin acts as an antagonist to MSH by causing the melanophores to contract (see page 722). In rats, melatonin has been reported to reduce the weight of the ovaries and to inhibit oestrus and sexual development^{8,9}; it also inhibits the increased frequency of oestrus observed in pinealectomized rats¹⁰. In human males, parenchymal-cell pineal tumours are associated with sexual retardation, whereas nonparenchymal tumours which destroy the pineal are associated with sexual precocity¹².

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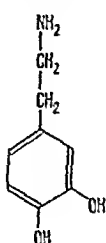
Catecholamines¹⁻⁴ (for references see page 734)

Chemistry

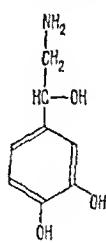
The catecholamines are phenylethylamine derivatives in which the benzene ring is orthodihydroxy-substituted, as in catechol. The most important members of this group are dopamine, noradrenaline and adrenaline. The catecholamines occur not only in the vertebrates but also in insects, where N-acetyldopamine also plays an important role⁵. The naturally occurring catecholamines are laevorotatory, the dextrorotatory forms being almost devoid of biological activity.

All the catecholamines have very similar chemical properties. Adrenaline and noradrenaline are oxidized spontaneously in alkali-

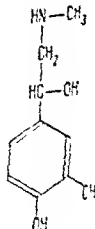
Dopamine
(3-hydroxytyramine)



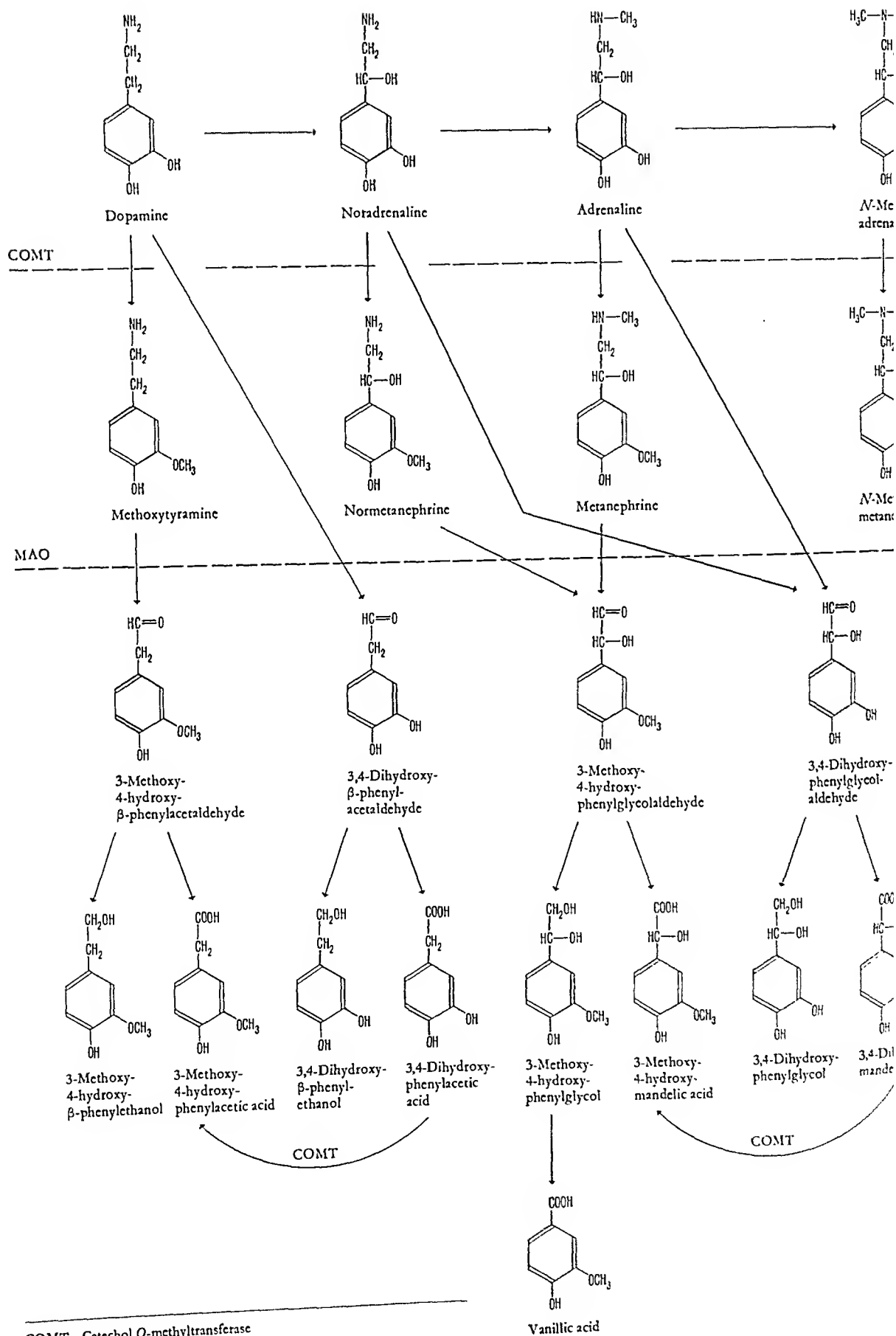
Noradrenaline
(norepinephrine)



Adrenaline
(epinephrine)



Metabolism of catecholamines



logical conditions and produces a rapid breakdown of glycogen to glucose 1-phosphate. Catecholamines appear to activate phosphorylase by a similar mechanism in all tissues. The lipolytic action of adrenaline and noradrenaline appears also to be mediated by cyclic AMP²⁷, but different forms of a triglyceride lipase have not yet been isolated.

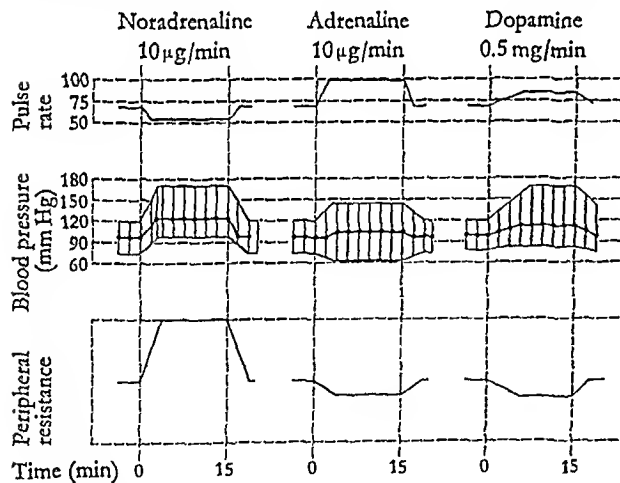
Pharmacological effects. Experimental studies have led to the idea of at least two kinds of adrenaline receptors, α and β ²⁸; α receptors mediate largely motor effects, β receptors largely the remaining effects. Noradrenaline acts on α receptors, isoprenaline on β receptors, adrenaline on both; adrenaline antagonists act primarily on α receptors. This is an oversimplified picture, and exceptions exist which have led to a further, though somewhat unprofitable, multiplication of postulated receptors.

Effects on blood circulation (see the figure below). In man, continuous intravenous infusion of catecholamines (0.1–0.3 $\mu\text{g}/\text{min}/\text{kg}$ body weight) can have the following effects⁴⁰: Noradrenaline. Prompt increase in the mean blood pressure of systolic and diastolic origin due to an increase in the peripheral resistance (vasoconstriction). Cardiac output unchanged or slightly diminished. Adrenaline. Increase in the mean blood pressure due to a fall in the blood pressure in the peripheral circulation (vasodilatation) being overcompensated by an increase in the beat volume and beat frequency. The circulatory effects of adrenaline and noradrenaline are mutually compensatory when the hormones are given at physiological dosage (intravenously up to 0.3 $\mu\text{g}/\text{min}/\text{kg}$ body weight).

The continuous intravenous infusion of dopamine at dosages in the range 5.3–11.6 $\mu\text{g}/\text{min}/\text{kg}$ body weight may result in an increase in the systolic and mean blood pressures and cardiac output and in a lowering of peripheral resistance⁴¹.

Renal blood flow is diminished by adrenaline⁴², large doses of which reduce the glomerular filtration rate. Adrenaline has little effect on the cerebral blood vessels.

Cardiovascular effects of intravenous infusion of noradrenaline, adrenaline and dopamine⁴³



Catecholamines in the central nervous system. Impulses arriving at the efferent ends of the sympathetic nerves cause the release of small amounts of noradrenaline which stimulate or inhibit cellular activity in the target organ (see above). Noradrenaline²⁷ and dopamine¹⁹ may exercise a similar function in the central nervous system. It has been suggested that in some kinds of depression, particularly the retarded type, there is a noradrenaline deficit at specific receptor sites in certain areas of the central nervous system; conversely, in manic states there would be an excess of noradrenaline in these areas³⁰.

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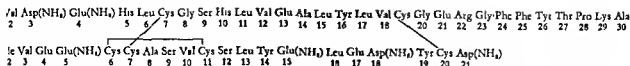
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Insulin^{1,2} (for references see page 737)

Chemistry

Up to 1966 the structure of insulins from 20 different animal species had been largely or wholly elucidated². In almost all species the shorter A chain contains 21 amino-acid residues and has an N-terminal glycine residue, at least four free amino groups and an internal disulphide bridge between the cysteine residues at positions 6 and 11. Variations in the amino-acid sequence are mostly in positions 8, 9 and 10. The longer B chain is made up of 28–30 amino-acid residues and contains two or three free amino groups and, in most species, an N-terminal phenylalanine residue. Variations in the amino-acid sequence in this chain are mostly in positions 3, 29

10-acid sequence of beef insulin



30. Of the 51 amino-acid positions in the insulin molecule, it is known to show variations. Human insulin differs from toad-insulin for instance in 17 of these positions. At least two species — rats and toadfish — form two structurally different insulins in the pancreas, while identical insulins may be formed by different species, for instance the dog, pig, fin whale and sperm whale.

Differences in the amino-acid sequences of various insulins

Species	A chain position			B chain position
	8	9	10	30
Man	Ala	Ser	Val	Ala
Pig	Thr	Ser	Ile	Ala
Sheep	Ala	Gly	Val	Ala
Horse	Thr	Gly	Val	Ala
Whale	Thr	Ser	Ile	Ala
Man	Thr	Ser	Ile	Thr

Insulin undergoes aggregation to form polymers of at least two molecules (insulin dimers). Whether this occurs in complex solutions of blood is not known. Insulin readily forms complexes with zinc and basic proteins such as histone and protamine. It crystallizes in solution or in the form of prisms. Heating of insulin solutions at pH < 3.5 results in the end-to-end aggregation of insulin monomers to form the characteristic insulin fibrils.

The insulins most commonly employed in the treatment of diabetes in man are those of bovine and porcine origin. Pig insulin differs from human insulin in only one amino-acid residue (B chain, position 30), beef insulin in three (A chain, positions 8 and 9, B chain, position 30). This difference in amino-acid structure may explain the greater antigenicity in man of beef insulin compared to pig insulin. In the light of its amino-acid structure, homologous insulin would not be expected to induce the formation of neutralizing antibodies. It has recently been shown, however, that injection of insulin from beef pancreas into cattle¹⁰ or of pig insulin into pigs¹¹ does in fact result in the formation of antibodies¹². Factors other than amino-acid sequence must therefore play a role in determining antigenicity.

Preparations of this kind with residual activity almost certainly contain intact insulin.

The complete synthesis of sheep insulin was achieved by three groups of workers at about the same time¹³; human insulin has also been synthesized¹⁴.

Protein 11 20 A minor component of pig insulin has been shown to be a single chain protein of 84 amino acids, this is converted into insulin by proteolytic cleavage. It cross-reacts with insulin in immunoassay.

Synthetic 12 12 An insulin-antagonistic factor migrating electrophoretically with albumin has been described (synalbumin insulin antagonist); the physicochemical properties of which suggest that it consists of the B chain of the insulin molecule.

The presence of an artifactual insulin antagonist in albumin preparations has been reported¹⁵.

Unit, methods of assay 16 15

1. Various methods of assay have been used for the determination of insulin activity in biological fluids.

living tissues. The preparations commonly used are the rat diaphragm, in which the index of insulin activity is glucose uptake or glycogen synthesis, and rat epididymal adipose tissue, in which the index can be glucose uptake, net gas exchange, oxidation of ¹⁴C-labelled glucose to ¹⁴CO₂, or incorporation of the labelled glucose carbon into lipid or adipose tissue glycogen. These methods of

Biosynthesis, secretion, metabolism

The biosynthesis of insulin in the pancreas is a complex process involving the transcription of DNA into RNA and the subsequent translation of the RNA into the insulin polypeptide chain.

1-4 IU/g¹⁶, the total amount being 100-400 IU with a mean of 250 IU (10 mg). From radioimmunological assays of plasma insulin the daily production of the pancreas has been estimated to be about 50 IU¹⁷; this corresponds to the daily average replacement dose in patients in whom endogenous production is completely suppressed.

Insulin secretion is stimulated or inhibited by a large number of factors¹⁸⁻²¹ (see the table on page 736).

Stimulation of insulin secretion has been observed in response to various stimuli, including glucose, amino acids, and certain hormones.

Insulin secretion is proportional to the amount of glucose flowing through the pancreas²², though it is probably not the glucose itself that has the stimulating action but a metabolite from the pentose-phosphate cycle²³. In man, the insulin level in the peripheral venous blood begins to rise within a few minutes of starting a glucose infusion²⁴.

The form in which insulin exists in the plasma is not known with certainty; it is generally assumed to be present as a monomer.

Factors affecting insulin secretion²⁴⁻²⁶

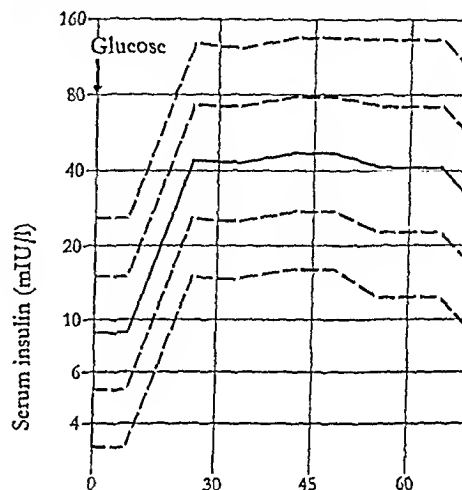
	In vivo	In vitro
<i>Factors stimulating secretion</i>		
Glucose.....	+	+
Fructose.....	+	+
Mannose.....	+	+
Ribose.....	+	+
Xylitol.....	+	+
Ribitol.....		+
Leucine.....	+	+
Arginine.....	+	+
Acetoacetate.....	+	±
Glucagon.....	+	+
Growth hormone.....	+	±
Lactogenic hormone of the placenta	+	
ACTH.....	+	+
Glucocorticosteroids.....	+	±
Thyroxine.....	+	±
Pancreozymin.....	+	
Secretin.....	+	+
Insulin antibodies.....	+	+
Calcium.....		+
Magnesium.....		±
Potassium.....	+	+
Adenosine triphosphate.....		+
Adenosine cyclic monophosphate..		+
Sulphonylureas.....	+	+
Vagus stimulation.....	+	
<i>Factors inhibiting secretion</i>		
2-Deoxyglucose.....	+	+
Glucosamine.....		+
Mannoheptulose.....	+	+
Adrenaline.....	+	+
Noradrenaline.....	+	
Insulin.....	+	
Phenethylbiguanides.....	+	
Diazoxides.....	+	+
Starvation.....	+	
Hypoxia.....		+
Vagotomy.....	+	

When serum is filtrated on Sephadex G-75, two protein peaks with a protein-free interval are obtained. Insulin-like activity is highest in the first protein fraction; insulin measured by immunoassay is highest in the 'protein-free' interval. This is also the area where labelled crystalline insulin is recovered²¹. When Sephadex G-50 is used for filtration, insulin appears in two peaks, designated 'big' and 'little' insulin, the first of which may be identical with pro-insulin²⁰.

Different methods of assay measure different amounts of insulin and/or insulin activity in the serum. The following mean values have been found in the morning in the serum of persons who have fasted for 12 hours previously: 20 mIU/l by the radioimmunological technique (see the table on this page), 100 mIU/l by the rat diaphragm method¹⁵ and 350 mIU/l by the rat adipose tissue method²¹. The insulin activity of the serum not inhibitable by insulin antibodies has been measured at about 170 mIU/l²². Serum insulin levels during the glucose-loading test are shown in the figure on this page. In pregnant women there is a rise in the serum insulin level towards term^{24,25}, and under glucose loading the level rises to a greater extent than post partum²⁴. In the serum of cord blood the insulin level is low²⁶. Small amounts of insulin have been detected in spinal fluid²⁷.

Plasma insulin determined by immunoassay (mIU/l in

	Mean	Range
Adults.....	20	0-66
Adults.....	20	6-35
Adults.....	22	-
Newborn, 2-8 days.....	43	-

Serum insulin after an oral dose of 50 g glucose²³
(values from 45 subjects, logarithmic scale)

Only part of the insulin secreted by the pancreas enters the general circulation, nearly a half of it being removed and degraded. In man the half-life in the circulating blood is 30 minutes, in animals rather less². Insulin also enters tissues, the highest concentrations of labelled insulin being found in the kidneys, liver and muscle. Small amounts are found normally in the urine; immunoassay of urine has shown an average of 5 mIU/24 h^{28,29}. Insulin in adults is about 0.4 ml/min^{28,29}; in children it is proportional to body weight and amounts to about 0.2 mIU/kg/24 h. Insulin filtered in the glomeruli is almost completely reabsorbed in the tubules, the daily turnover being about 14 mIU/l²⁸. Degradation of insulin is probably also in the kidneys and other tissues by a specific enzyme, protein disulphide reductase, which breaks the disulphide bonds to free the A and B chains³⁰, which are then attacked by proteolytic enzymes. During pregnancy the placenta is also involved in the breakdown of insulin.

Biological activity

Insulin has a direct or indirect effect on practically all metabolic processes of the body. The most obvious effects are on those most thoroughly studied, are on the fatty tissues and liver⁴⁵. Various theories have been put forward to explain its mode of action, which may well vary from site to site: (a) the insulin-enzyme theory, (b) the insulin-transport theory, (c) the insulin-gene (transcription) theory and (d) the insulin-ribonucleic acid (RNA) theory. For further details see the literature⁴⁶.

The most important role of insulin is in the metabolism of the fatty tissues, the principal site of the regulation of energy storage and mobilization. Insulin promotes storage of fat and release. The hormone stimulates glucose uptake and glucose metabolism in the fatty tissues as well as the formation of glyceride, fatty-acid synthesis, glucose, transamination of glucose into amino acids, and protein synthesis; it inhibits the release of fatty acids by promoting the release of α -glycerophosphate, with which they form triglycerides.

In muscle, insulin activates the transport system responsible for the entry of amino acids and other compounds into the cell. Glucose is converted into glucose 6-phosphate by hexokinase and finally into glycogen by activation of glycogen synthetase. Activation of the transport of amino acids proceeds independently of that of glucose.

glucagon content of the pancreas, whereas damage to the α -cells by cobalt chloride or other compounds causes a gradual diminution of glucagon activity. Glucagon can be isolated from those parts of the dog pancreas which contain α -cells but is not found in the uncinate process, where α -cells are lacking. Furthermore, in different species the amount of extractable glucagon in the pancreas correlates well with the relative abundance of α -cells in the organ. Histochemically, tryptophan, a component of glucagon but not of insulin, can be demonstrated in α -cells but not in β -cells¹. More direct evidence in favour of the α -cell origin of glucagon has been obtained recently with specific immunofluorescence techniques¹¹.

Both the muscular and mucosal layers of dog and human upper gastrointestinal tract have been found to contain significant amounts of a glucagon-like substance in measurements made by the method of liver adenylyl cyclase assay¹⁰. A glucagon-like substance was also detected in the gastrointestinal tract by radioimmunoassay¹². This technique reveals a glucagon content in the human pancreas of 4.0–12.4 $\mu\text{g/g}$ and a content of glucagon-like substance in the human colon of 0.006–0.01 $\mu\text{g/g}$; the glucagon-like immunoreactivity of the whole digestive tract probably does not amount to more than 25–50% of that of the pancreas. Glucagon has also been identified radioimmunochemically in acid alcohol extracts of an undifferentiated bronchogenic carcinoma¹³. There is no evidence to suggest that glucagon is related to hyperglycaemic substances isolated from skin, lymph glands, tongue and spleen.

Published data on the plasma glucagon level in fasting subjects vary from 0.1 $\mu\text{g/l}$ to 5 $\mu\text{g/l}$; more recent publications indicate that it is below 0.3 $\mu\text{g/l}$ ¹⁴. The glucagon content of the blood increases in starvation, insulin-induced hypoglycaemia, and phlorizin diabetes; administration of glucose to phlorizin-treated animals or persons with hypoglycaemia causes the blood glucagon level to fall^{6,15}. Paradoxically, oral glucose loading also causes a rapid rise in the blood glucagon level, an effect that occurs to only a small extent when glucose is given intravenously¹⁶. This glucagon-like immunoreactivity probably arises from the gut¹⁶. In the blood, glucagon does not appear to be bound to plasma proteins¹⁷.

Glucagon is degraded by the kidneys, liver and other organs and to some extent in the blood. Following injection of glucagon labelled with ¹³¹I, the hormone becomes concentrated in the following organs (in decreasing order of amount stored): kidneys, liver, pituitary, spleen, lungs, salivary glands, adrenals, pancreas, thyroid, heart, duodenum, lymph glands. Hepatectomy and nephrectomy show that the liver and kidneys are the main sites of degradation of glucagon, in which a proteolytic 'glucagonase' of limited specificity is said to take part. This enzyme contains SH groups and is inhibited by insulin, growth hormone, α -ACTH and α -cascien. Injected glucagon is thus quickly broken down – in man it has a half-life of less than 10 min⁷ – so that it is therefore unlikely to be identical with the glycogenolytic or hyperglycaemia-producing substances found in the urine of normal individuals, diabetics and schizophrenics.

Biological activity

Long-continued administration of neutral red results in degranulation of the pancreatic α -cells and a reduction in their absolute number. Rats treated in this fashion develop fasting hypoglycaemia and subnormal tolerance to insulin and tolbutamide¹⁸.

Glucagon administration to mammals, birds and reptiles causes a rise in the blood glucose concentration. The magnitude of the rise and its duration depend on the dose, the mode of administration, the nutritional state of the subject and the species of animal being tested. This hyperglycaemic effect is maximal in fed animals with plentiful hepatic glycogen reserves, is diminished but not abolished when hepatic glycogen stores are depleted, and is absent in the eviscerated animal. The hyperglycaemia induced by glucagon is accompanied by rapid depletion of hepatic glycogen stores in vivo. In vitro (isolated perfused liver, liver slices, liver homogenates) glucagon is a potent glycogenolytic agent in physiological concentrations¹. Conversely, glucagon stimulates gluconeogenesis from amino acids and lactate in the perfused rat liver^{19,20}. When these substrates are not provided it promotes new glucose formation from endogenous liver protein²¹. Glucagon has an inotropic effect on the heart, where it enhances oxidation of glucose and acetate to CO_2 ²².

The manner in which glucagon intervenes in carbohydrate metabolism has been largely elucidated. Like adrenaline (see page 733), glucagon stimulates the formation of adenosine cyclic 3',5'-phosphate²³ and therefore increases glycogenolysis. This biomolecular action of glucagon has been observed in the liver and heart but –

in contrast to adrenaline – not in skeletal muscle². The action of adenosine cyclic 3',5'-phosphate, and of glucagon, in stimulating gluconeogenesis from lactate in the perfused rat liver probably takes place through activation of phosphopyruvate carboxylase²⁰. Glucagon causes a significant release of potassium from the liver. This phenomenon precedes phosphorylase activation, but it is uncertain whether the two effects are related²⁴.

Glucagon is antagonistic to insulin in that it promotes the release of glucose in the liver in hypoglycaemia²⁵; on the other hand it also appears to stimulate insulin secretion in man independently of its hyperglycaemic effect²⁶. When added to rabbit pancreatic slices it causes release of insulin into the incubation medium, the reaction rate increasing with the glucose concentration of the medium²⁷. In man under physiological conditions it is possible that pancreatic glucagon is primarily insulinogenic and secondarily hyperglycaemic, whereas the glucagon of the digestive tract is primarily hyperglycaemic¹².

When given to animals in large doses over long periods, glucagon produces hyperglycaemia, glycosuria, a markedly negative nitrogen balance, weight loss and increased basal metabolic rate, while in at least one species (rabbit) it may induce permanent diabetes (metaglycaemia diabetes)²⁸. There is no evidence, however, indicating that hypersecretion of glucagon is a pathogenic factor in diabetes.

Glucagon diminishes gastrointestinal motility²⁹, inhibits the secretion of gastric juice and hydrochloric acid², and abolishes hunger². In the kidneys it has a diuretic action and increases the excretion of sodium, potassium, chloride, bicarbonate, phosphate and uric acid^{2,30}. Here glucagon may again act by producing adenosine cyclic 3',5'-phosphate, which may be capable of changing the permeability of the nephron (see under 'Oxytocin and Vasopressin', page 723).

A further action of glucagon is on lipid metabolism, in that the hormone promotes mobilization of fatty acids from adipose tissue³¹. Once again the underlying mechanism is probably the formation of adenosine cyclic 3',5'-phosphate (see under 'Catecholamines', page 733).

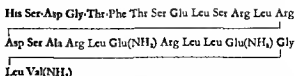
Clinical significance

Insufficient endogenous glucagon secretion has been postulated as a cause of hypoglycaemia in certain patients in whom histological examination of the pancreas showed it to be deficient in α -cells, but this remains to be confirmed by measurements of pancreatic glucagon content and serum levels of the hormone in this type of patient³². A pancreatic islet cell tumour in which immunoassay revealed large amounts of glucagon has been reported, the patient having high serum glucagon and insulin levels and mild diabetes³³. The full syndrome of glucagon excess as produced experimentally in animals has not yet been shown to occur spontaneously in man.

Diagnostically, glucagon is useful in the evaluation of patients with glycogen storage disease. Depending on the position of the enzymatic block in the glycogenolytic pathway, the hyperglycaemic effect of glucagon may be absent, normal, blunted, or present only shortly after a carbohydrate meal. Atypical results, however, have been reported. The response to glucagon has also been used to evaluate glycogen reserves in Addison's disease, diabetes and liver disease. In pharmacological doses glucagon stimulates myocardial contractility and the heart rate, an effect which suggests therapeutic possibilities in congestive heart failure³⁶.

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This polypeptide has been synthesized and the synthetic hormone shown to have quantitatively the same physiological properties as highly purified secretin from swine.

Secretin is released on acid stimulation of the duodenum and plays an important part in neutralization of the contents of the small intestine. It increases the blood flow to the pancreas, and in this organ stimulates not only the exocrine secretion of water (see page 651) and bicarbonate (see page 652) but also the endocrine secretion of insulin¹⁸. Secretin stimulates the flow of bile by favouring the production of a fluid rich in bicarbonate²⁰.

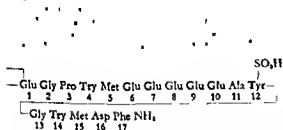
Secretin has been shown by radioimmunoassay to be present in normal human serum at a concentration of less than 0.4 µg/l in fasting and up to 25 µg/l after oral glucose loading¹⁹.

Cholecystokinin-pancreozymin

hormones of the gastrointestinal tract²

trins^{2,3}

hormones of the gastrointestinal tract



Gastrin I differs from gastrin II in having no sulphate group attached to the tyrosine residue. The human gastrins are distinguished from the porcine compounds by having a leucine instead methionine residue at position 5⁴. The structure of the canine

Cholecystokinin-pancreozymin has the same spectrum of biological activity as gastrin but its effects differ markedly in intensity compared to the latter. It is a very weak stimulant of gastric acid secretion, but unlike gastrin it causes strong contractions of the gall-bladder. The exocrine discharge of enzymes by the pancreas is stimulated (see page 652), but the hormone has no effect on the amount of pancreatic juice secreted or on its bicarbonate content. Cholecystokinin-pancreozymin also stimulates the secretion of insulin and glucagon¹⁸.

Enterogastrone

This hormone is present in the mucosa of the small intestine but has not yet been isolated. Its release is stimulated by contact of fats and sugars with the mucosa of the small intestine. The hormone is thought to inhibit the secretory and motor activity of the stomach.

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me¹³ Gastrin is released on stimulation of the vagus nerve, on contact of food with the pyloric antrum, and on dilation of the antrum. Acetylcholine liberated from the nerves acts as inter-

ghet dose of gastrin¹⁸. At high dosages, which inhibit acid secretion, gastrin stimulates the secretion of pepsin, it also increases

Secretin originates from the mucosa of the upper small intestine and is a polypeptide consisting of 27 amino-acid residues with the following structure

Erythropoietin¹

Erythropoietin is a factor easily demonstrable in the serum of various animal species under certain circumstances (hypoxia, anaemia, injection of cobalt chloride); it has been shown to stimulate erythropoiesis in a specific fashion. It appears to be a mucopolysaccharide or glycoprotein containing sialic acid and has a reported molecular weight of 10000-62000^{2,3}. Erythropoietin possesses weak antigenic properties⁴.

Erythropoietin can be detected in vivo by studying erythropoiesis (⁵¹Fe-incorporation in erythrocytes, reticulocytosis) in mice or rats in which this function is suppressed. Its in vitro determination (for instance in bone-marrow cultures) has proved less successful. An immunoassay method has recently been developed¹⁶.

1 International Unit (IU) of erythropoietin is contained in 1.48 mg of the 1st International Reference Preparation (see page 763). This unit is the same as the unit of the Erythropoietin Standard A or B of the National Institute for Medical Research, London⁵. Highly purified preparations from rabbit plasma or human urine have an activity up to 368 IU/mg³.

The kidneys play a particular role in the formation of erythropoietin, which is either mainly produced in this organ⁶ or is the result of the formation by the kidneys of an enzyme (renal erythropoietic factor) that liberates erythropoietin from the plasma proteins⁷. Erythropoietin formation is elicited by oxygen deficiency in the tissues and may be stimulated by the androgens⁸, which would account for the higher erythrocyte count in men.

Erythropoietin is barely detectable in normal human plasma by biological methods⁹, but immunoassay has revealed a concentration of 7-30 U/l¹⁶. The hormone disappears fairly rapidly from the circulating blood, the half-life being about 2-3 hours¹⁰. Normal values for the urinary excretion are given in the table below; discrepancies in reported values can probably be ascribed to differences in methods of measurement. The acceleration of erythropoiesis during pregnancy is associated with increased erythropoietic activity in the plasma and, in the second trimester, in the urine¹¹. High levels of erythropoietic activity are found in cord blood¹², and erythropoietin has also been detected in the amniotic fluid¹³. Increased amounts of erythropoietin have been demonstrated in the plasma of many patients with polyglobulism, anaemia, blood loss or haemolysis^{9,14}.

Urinary excretion of erythropoietin (IU/24 h)

	Mean	Range	s	Reference
Boys	1.0	0.6-1.2	-	17
Men	2.8	1.5-5.2	1.3	17
Women	0.9	0.5-1.8	0.4	17
Men	0.54	0.21-1.2	-	18
Women	0.22	0.16-0.32	-	18
Men in Chacaltaya, Bolivia (5200 m)	9.1	1.1-22.4	-	18

Biological activity

Erythropoietin stimulates proliferation of the erythroblasts in the bone marrow, increases the numbers of reticulocytes and erythrocytes in the peripheral blood and promotes the metabolism of the bone marrow, reticulocytes and erythrocytes (purine synthesis, haem synthesis, DNA synthesis, RNA synthesis)¹⁵.

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¹³ FINNE, P.H., *Brit. med. J.*, **1**, 697 (1965).

¹⁴ MOVASSAGHI et al., *Proc. Soc. exp. Biol. (N.Y.)*, **126**, 615 (1967).

¹⁵ REMMELE, W., *Die humorale Steuerung der Erythropoiese*, Springer, 1963; PIEDER-PERRETTA et al., *Biochim. biophys. Acta (Amst.)*, **95**, 360 (1963); RUDOLPH and PERRETTA, *Proc. Soc. exp. Biol. (N.Y.)*, **124**, 1041 (1967).

¹⁶ POWSNER and BERMAN, *Blood*, **30**, 189 (1967).

¹⁷ LANGE et al., *J. Lab. clin. Med.*, **73**, 78 (1969).

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Renin-angiotensin system^{1,2}

Chemistry

This system consists of a complex enzymatic reaction in which the enzyme renin acts on a plasma protein substrate (angiotensinogen) to liberate the decapeptide angiotensin I (hypertensin I, or tonin I). This latter substance is broken down to the octapeptide angiotensin II by the action of a plasma enzyme complex (converting enzyme) activated by chloride. Angiotensin II is in turn rapidly converted into inactive peptides by peptide hydrolases ('angiotensinase') present in the tissues (kidneys, liver), erythrocytes plasma, its half-life in the blood being about 1 min. These react are subject to the action of various activators and inhibitors present in the plasma.

Renin is a protein with a molecular weight of about 43000 (man)³, angiotensinogen a plasma protein belonging to the globulin group. The latter is converted by trypsin into a tetradecapeptide, the so-called polypeptide renin substrate, which is split by renin at the Leu-Leu linkage. The structures of this compound and of the angiotensins are shown in the table opposite. The synthetic Val¹-angiotensin-II-Asp¹-β-amide has the same qualitative and quantitative pharmacological properties as naturally occurring angiotensin II⁴ and is therefore suitable for use as reference substance.

Units

Renin. 1 GOLDBLATT Unit is the amount of renin that increases the mean arterial blood pressure (measured directly in the femoral artery) by 30 mm Hg when injected intravenously into nonanaesthetized dogs¹. By using angiotensinogen as substrate, renin concentration can be expressed as enzyme activity, 1 unit corresponding to the formation of 1 ng angiotensin per minute^{5,6}.

Angiotensin. 1 GOLDBLATT Unit is the amount of angiotensin that increases the mean arterial blood pressure (measured directly in the femoral artery) by 30 mm Hg when injected intravenously in nonanaesthetized dogs¹. Angiotensin concentration can also be expressed in terms of the reference substance angiotensin II (see above), 1 μg angiotensin II corresponding to about 2.2 GOLDBLATT Units⁷.

Methods of assay

Renin

Biological methods. (a) Direct measurement of the hypertensive effect in vivo after intravenous injection of the test solution in nonanaesthetized dogs¹ or in vitro in an aorta preparation⁸. (b) Method of BOCHER et al.⁵ for plasma renin (renin-like activity). Incubation of the plasma containing renin and angiotensinogen together with activators and inhibitors at pH 5.5 and 37°C in the presence of Dowex 50W-X2(NH₄), an ion-exchange resin that adsorbs angiotensin and thus prevents its breakdown by angiotensinase; after elution the angiotensin is determined by its hypertensive effect on rats. (c) Method of BROWN et al. for plasma renin⁶. After adsorption of the renin in a DEAE-cellulose column and subsequent elution the angiotensinogen and 'angiotensinase' are eliminated by acidification; the renin so isolated is incubated with bovine angiotensinogen at pH 5.7 and 37°C and the angiotensin liberated determined by its hypertensive effect on rats.

Chemical methods. Fluorimetric determination of the hydrolysis products in a synthetic substrate acted on by renin⁹. This method is too insensitive for assay of the renin content of plasma.

Structure of angiotensins

	Mol wt	Amino-acid sequence	Origin
Ile ⁶ -polypeptide-renin substrate	1759	Asp Arg-Val-Tyr Ile His Pro-Phe His Leu Leu Val Tyr Ser 1 2 3 4 5 6 7 8 9 10 11 12 13 14	Equine plasma after action of trypsin ²⁶
Ile ⁶ -angiotensin I	1297	Asp-Arg-Val-Tyr Ile-His-Pro-Phe His Leu 1 2 3 4 5 6 7 8 9 10	Equine ²⁷ , porcine ²⁸ , human ²⁹ plasma
Val ⁶ -angiotensin I	1283	Asp Arg Val Tyr Val His Pro Phe His Leu 1 2 3 4 5 6 7 8 9 10	Bovine plasma ³⁰
Ile ⁶ -angiotensin II	1046	Asp Arg Val Tyr-Ile His Pro Phe 1 2 3 4 5 6 7 8	From Ile ⁶ -angiotensin I
Val ⁶ -angiotensin II	1032	Asp Arg Val Tyr Val His Pro Phe 1 2 3 4 5 6 7 8	From Val ⁶ -angiotensin I
Val ⁶ -angiotensin-II-Asp ¹ -β-amide	1029	Asp(NH ₂) Arg Val-Tyr Val His Pro-Phe 1 2 3 4 5 6 7 8	Synthetic ⁴

Angiotensin

Biological methods. (a) Direct measurement of the hypertensive effect *in vivo* after intravenous injection of the test solution into nonanaesthetized dogs¹ or *in vitro* in an aorta preparation².

sterone production selectively³¹. The rate of aldosterone secretion is a direct function of the plasma renin activity which is

The renin-angiotensin system appears to be involved in the thirst mechanism since both these substances have been shown to instigate drinking to replace lost fluid³². Angiotensin regulates renin secretion through a negative feedback mechanism³⁴.

Clinical significance

Measurement of plasma renin activity enables a distinction to be made between primary aldosteronism (decreased renin activity) and secondary aldosteronism (increased renin activity). It can also be used to confirm the renovascular origin of arterial hypertension associated with renal arterial stenosis.

Test of KAPLAN and STAN²⁸. Sensitivity to the hypertensive effect of an intravenous infusion of angiotensin is decreased in renovascular arterial hypertension, increased in primary aldosteronism.

Renin and angiotensin contents of blood

	Mean	Range	s	Method	Reference
Renin (U/l)					
Plasma	9.0	0-32	7.6	Biological	14
Plasma	4	2-10	-	Biological	33
Angiotensin (ng/l)					
Plasma	60	-	100	Biological	34
Blood	95	-	66	Biological	35
Plasma	-	<8-56	-	Radioimmunological	36
Blood	21	-	14	Radioimmunological	37

Biological activity

The active agent in the renin-angiotensin system is free angiotensin II, which has three main effects¹⁸

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³² FITZSIMONS, J. T., *J. Physiol.*, **201**, 349 (1969).
³³ KLAUS et al., *Dtsch. med. Wschr.*, **92**, 2114 (1967).
³⁴ GENEST et al., *Canad. med. Ass. J.*, **90**, 263 (1964).
³⁵ ZULEMA et al., *Clin. Sci.*, **30**, 473 (1966).
³⁶ BORD et al., *Lancet*, **2**, 1002 (1967).
³⁷ CATT et al., *Lancet*, **2**, 1005 (1967).

Plasma kinins¹⁻³

Chemistry

The kinins are low-molecular polypeptides of high pharmacological activity arising from the action of proteolytic enzymes on the plasma proteins. Naturally occurring kinins that have also been synthesized are listed in the table below.

The kinins are best detected by means of their contractile action on the isolated guinea-pig ileum or on the isolated uterus of the rat in full oestrus. Bradykinin can be determined by radioimmunoassay by means of its ¹⁴C-acetyl derivative⁴.

Biosynthesis, metabolism

The inactive precursors of the kinins, the kininogens, are α_2 -globulins with a molecular weight of about 50 000. These give rise to the plasma kinins through the action of the enzyme kallikrein. A kininogen isolated from bovine serum yielded 20 μ g bradykinin/mg⁵. The enzyme kallikrein occurs in urine, sweat, saliva and faeces, its inactive precursor prekallikrein (kallikreinogen) in the pancreas, salivary glands, gut wall, tongue and plasma². In blood, kallikrein is liberated from prekallikrein in the presence of factor XII (HAGEMAN factor). Free kallikrein is inhibited by substances in various tissues, particularly the lungs and salivary glands.

In blood the kinin kallidin is rapidly converted into bradykinin by an aminopeptidase. In the plasma of adults the bradykinin level is less than 2 μ g/l⁶; in cord blood the mean level is 12.8 μ g/l⁶. Higher values occur in shock, acute pancreatitis and the carcinoid syndrome^{2,7}. The plasma kinins are rapidly broken down by peptidases into inactive fragments⁷. Kinin-inactivating enzymes are present in many tissues, for instance in the liver, spleen, kidneys, lungs and lymph glands. When injected intravenously bradykinin is metabolized in the blood with a half-life of 30 s⁸. Urine contains two urokinins with a pharmacological activity resembling that of bradykinin and kallidin, but these probably originate not in the blood but in the epithelium of the renal tubules⁹.

Biological activity

The plasma kinins have a contractile effect on smooth muscle, for instance that of the gut, uterus and bronchi, and lower the blood pressure and increase vascular permeability when given intravenously; they cause pain when applied to the base of a can-

tharides blister. The effect of bradykinin on the isolated α is about the same as that of oxytocin². The blood pressuring effect is due to dilation of the resistant vessels; the minute volume and regional blood flow are all increased.

The physiological function of the kinins is not known, but in the regulation of the blood flow to the secretory glands suggested¹⁰. Bradykinin is possibly involved in the transition from foetal to newborn circulation⁶.

The plasma kinins play a role in two diseases, hereditary neurotic oedema, due to a dominantly inherited, congenital deficiency of plasma kallikrein inhibitors¹¹, and the carcinoid, in which the flush-producing principle is identified as bradykinin¹². The role played by the plasma kinins in inflammatory reactions remains obscure, but it seems that the kinin system is activated wherever tissues are damaged¹⁴. Kinin has been detected in the synovial fluid of patients with arthri-

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⁴ RINDERKNECHT et al., *Nature*, **213**, 1130 (1967).
⁵ HABERMANN, E., *Biochem. Z.*, **337**, 440 (1963).
⁶ MELMON et al., *J. clin. Invest.*, **46**, 1094 (1967).
⁷ ERDÖS, E. G., *Gastroenterology*, **51**, 893 (1966).
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¹⁰ HILTON and LEWIS, *Brit. med. Bull.*, **13**, 189 (1957).
¹¹ LANDERMAN et al., *J. Allergy*, **33**, 330 (1962).
¹² OATES et al., *Lancet*, **1**, 514 (1964); OATES et al., *J. clin. Invest.*, **45**, 17.
¹³ SCHROEDER and LUECKE, *The Peptides*, vol. 2, Academic Press, New York, 1966.
¹⁴ LEWIS, G. P., in ROBSON and STACEY (Eds.), *Recent Advances in Pharmacology*, 4th ed., Churchill, London, 1968, page 213.

Corticosteroids

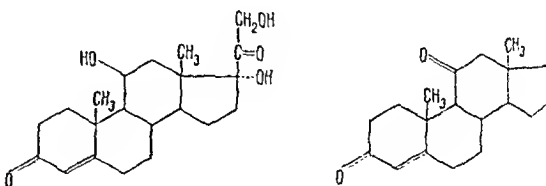
(adrenocortical hormones) (for references see pages 750-751)

Chemistry

The corticosteroids consist of C₂₁-steroids containing a three oxygen atoms and are present in the adrenal cortex, and urine¹. The structural formulae of the seven most important biologically active corticosteroids are shown below. Biological activity requires the presence of the Δ^4 -3-keto configuration A and of a keto group in the side chain. Characteristic of steroid is the aldehyde group (C-18). Other steroids formed in the adrenal cortex are pregnanetriol and the androgens dehydroepiandrosterone, androstenedione and 11 β -hydroxyandrostenedione.

Cortisol (hydrocortisone)

Cortisone



Structure and biological activity of naturally occurring plasma kinins¹³

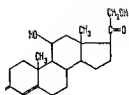
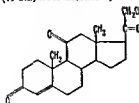
	Mol. wt.	Structure	Relative activity		Occurrence
			in vitro*	in vivo**	
Bradykinin (kallidin I, kallidin-9, kinin-9)	1060	Arg-Pro-Gly-Phe-Ser-Pro-Phe-Arg	100	100	Bovine plasma, human plasma
Kallidin (kallidin II, lysylbradykinin, kinin-10)	1188	Lys-Arg-Pro-Gly-Phe-Ser-Pro-Phe-Arg	33	190	Bovine plasma, human plasma
Methionylkallidin (methionyl-lysylbradykinin, kinin-11)	1329	Met-Lys-Arg-Pro-Gly-Phe-Ser-Pro-Phe-Arg	25	-	Bovine plasma

* Contraction of the isolated guinea-pig ileum.

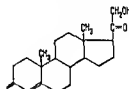
** Lowering of blood pressure in rabbits.

(For references see pages 750-751)

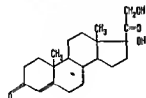
Corticosterone

Dehydrocorticosterone
(11-dehydrocorticosterone)

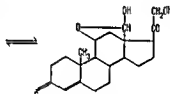
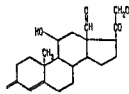
Deoxycorticosterone (cortisone)



11-Deoxycortisol (cortisolone)



Isoflutrone

Assay²

The hormones must first be extracted from the tissue by means of a suitable solvent. During extraction and subsequent operations care must be taken to avoid the formation of artefacts, either as a result of autooxidation in air or of the techniques employed.

By using group-specific methods, various classes of steroids can be determined (see the table on page 744).^{3,4} If the individual

veloped⁵

used for cortisol and cortisone. Pregnenetriol can be determined by the methods of DONOVANNI and ESALZIN¹² or HARKNESS and LOVE¹³, dehydroepiandrosterone by the method of FORTNEY¹⁴.

The many biological methods for assay of corticosteroids (for a review see DONOVANNI¹²), while no longer of clinical interest, are useful for

nalectomized rats after injection of these isotopes¹⁵

Biosynthesis, secretion, metabolism

Of the steroids formed in the adrenal cortex, those affecting salt and water balance (aldosterone and, less active in this respect, corticosterone) originate in the outermost layer (zona glomeru-

losa), those affecting carbohydrate metabolism (cortisol, cortisone and, less active in this respect, corticosterone) in the middle layer (zona fasciculata), and the 17-sterosteroids (mainly dehydroepiandrosterone) in the innermost layer (zona reticularis).

The pattern of corticosteroids secreted differs from one animal species to another. In man, those secreted in the largest amounts are cortisol and corticosterone. The cortisol/corticosterone ratio in the venous blood of the adrenals is 0.5-5, in the peripheral blood 5-30, the difference being due to the more rapid breakdown of corticosterone¹⁶.

(continued on page 745)

Rates of secretion of corticosteroids

	Mean	Range	s	Reference
Aldosterone (μg/24 h)				
Newborn	23	9-41	12	78
Infants	72	25-138	29.5	78
Children, 1-15 years	91	57-162	30.4	78
Adults ..	80	39-138	30.8	78
Adults ..	135	70-210	-	78
Men, 18-35 years ..	77	40-110	-	77
Men, 67-83 years ..	34	20-72	-	77
Women, proliferative phase ..	139	-	44	78
Women, luteal phase ..	235	-	101	78
Women, pregnant ..	-	387-2912	-	78
Corticosterone (mg/24 h)				
Adults ..	2.3	1.5-4.0	-	80
Adults ..	3.22	2.1-4.2	-	81
(mg/24 h/m² body surface)				
Infants up to 3 months ..	2.5	-	-	82
Children ..	0.65	-	-	82
Cortisol (mg/24 h)				
Infants up to 3 months ..	3.8	-	-	82
Children ..	16	8.5-22.5	-	82
Adults ..	-	4.9-27.9	-	84
Adults ..	16.0	10.5-23.5	-	81
Women ..	17.5	11.4-20.9	1.9	85
Men ..	21.0	15.9-27.4	3.1	85
Old men ..	17.7	12.3-23.0	-	86
Pregnant women ..	15.0	11.3-18.9	-	86
(mg/24 h/m² body surface)				
Newborn, up to 5 days ..	18.7	-	3.7	87
Infants, 5-20 days ..	13.9	-	2.9	87
Persons, 4 months-20 years ..	12.1	-	2.9	87
Dehydroepiandrosterone sulphate (mg/24 h)				
Women ..	12	10-18.5	-	88
Men ..	17	14-22	-	88
Deoxycorticosterone (μg/24 h) ..				
..	-	50-160	-	89
11-Deoxycortisol (mg/24 h) ..				
..	-	0.20-2.0	-	90
11-Hydroxycorticosterone (μg/24h)				
..	305	145-460	-	78

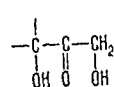
Corticosteroid content of the normal adrenal gland¹⁷

	μg/g tissue	
	Mean	Range
Aldosterone	0.06	0.05-0.08
Corticosterone	1.7	0.75-2.9
Cortisol	2.7	0.97-3.9
Cortisone	0.05	0-0.10

Group-specific methods of corticosteroid assay

Steroid class	Specific chemical structure	Method	Reference
PORTER-SILBER chromogens.....	17,21-Dihydroxy-20-keto (dihydroxyacetone) side chain (see below)	Colour reaction with phenylhydrazine in ethanolic sulphuric acid	PORTER and SILBER ⁶¹ , PETERSON et al. ⁶²
21-Deoxyketols.....	17-Hydroxy-20-keto-21-deoxy side chain (see below)	Specific oxidation to 17-ketosteroids followed by ZIMMERMANN's reaction (see under '17-Ketosteroids' below) Vanillin-phosphoric acid method	APPLEBY and NORYMBERSKI ⁶³ McALEER and KOZŁOWSKI ⁶⁴
17-Ketogenic steroids.....	Side chain as shown below	Specific oxidation to 17-ketosteroids followed by ZIMMERMANN's reaction (see under '17-Ketosteroids' below)	NORYMBERSKI et al. ⁶⁵
Total 17-hydroxycorticosteroids.	Side chain as shown below	Specific oxidation to 17-ketosteroids followed by ZIMMERMANN's reaction (see under '17-Ketosteroids' below)	APPLEBY et al. ⁶⁶ , FEW ⁶⁷
17-Deoxycorticosteroids.....	17-Deoxy-20-keto-21-hydroxy side chain (see below)	Specific oxidation to aldehydes and colour reaction of hydroxamic acids	ENLEY et al. ⁶⁸
Reducing corticosteroids.....	20-Keto-21-hydroxy side chain (α -ketol group)	Alkaline reduction of blue tetrazolium to a coloured diformazan	MADER and RUCK ⁶⁹
11-Hydroxycorticosteroids.....	Δ^4 -11-Hydroxy configuration	Fluorescence in ethanolic sulphuric acid	MATTINGLY ⁷⁰ , SILBER ⁷¹
Δ^5 -3 β -Hydroxysteroids.....	Δ^5 -3 β -Hydroxy configuration (e.g., pregnenolone, but not cholesterol)	Colour reaction in ethanolic sulphuric acid	OERTEL and EIK-NES ⁷²
Δ^4 -3-Ketosteroids.....	α,β -Unsaturated ketones	Colour reaction with isonicotinic hydrazide	UMBERGER ⁷³
17-Ketosteroids.....	Contain $-\text{CO}-\text{CH}_2-$ group; the 17-keto group is the most reactive	Colour reaction with <i>m</i> -dinitrobenzene in alkaline solution	ZIMMERMANN ⁷⁴

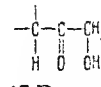
Structure of steroid side chains



PORTER-SILBER chromogens



21-Deoxyketols



17-Deoxycorticosteroids

17-Ketogenic steroids

Total 17-hydroxycorticosteroids

secreted steroids as a result not only of metabolic action but also of the analytical procedures. Best results are given by isotope dilution techniques^{19,20}

In health, the normal adult secretes 5-28 mg cortisol per day

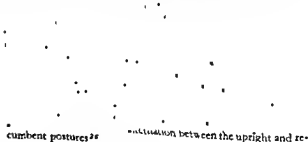
Corticosteroids in plasma (μg/l)

	Mean	Range	n	Reference
Aldosterone				
Men	0.06	0.02-0.15	-	21
Adults	0.22	0.06-0.59	-	27
Corticosterone				
Cord blood	53	-	33	22
Children, 3-7 days	63	-	41	22
Children, 3 months-5 years	45	-	22	22
Children, 11-17 years	36	-	24	22
Adults	36	-	18	22
Adults	11	5-20	3	23
Cortisol				
Newborn, up to 12 hours	71	33-198	315	24
Infants, 12-24 hours	38	10-107	300	24
Infants, 36-48 hours	42	15-66	235	24
Infants, 1-5 months	47	38-62	104	24
Cord blood	129	-	47	22
Infants, 3-7 days	140	-	48	22
Children, 3 months-5 years	124	-	50	22
Children, 11-17 years	124	-	54	22
Adults	117	-	27	22
Adults	150	-	-	23
Adults	-	21-226	-	25
Cortisone				
Newborn, up to 12 hours	53	24-97	224	24
Infants, 12-24 hours	45	24-96	190	24
Infants, 36-48 hours	39	20-60	135	24
Infants, 1-5 months	6	0-9	40	24
11-Deoxycortisol	-	0-14	-	25
Progesterone	-	<50	-	26

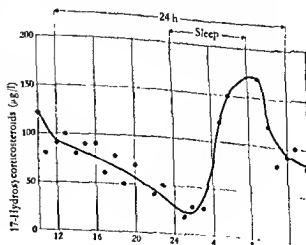
Corticosteroid fractions in plasma (μg/l)²⁶

	Mean	s
Porter-Silber chromogens		
Unconjugated....	129	43
Conjugated...	173	56
Δ⁴-3-Ketosteroids		
Unconjugated...	133	49
Conjugated...	118	63
Reducing corticosteroids		
Unconjugated.....	216	59
Conjugated.....	750	248

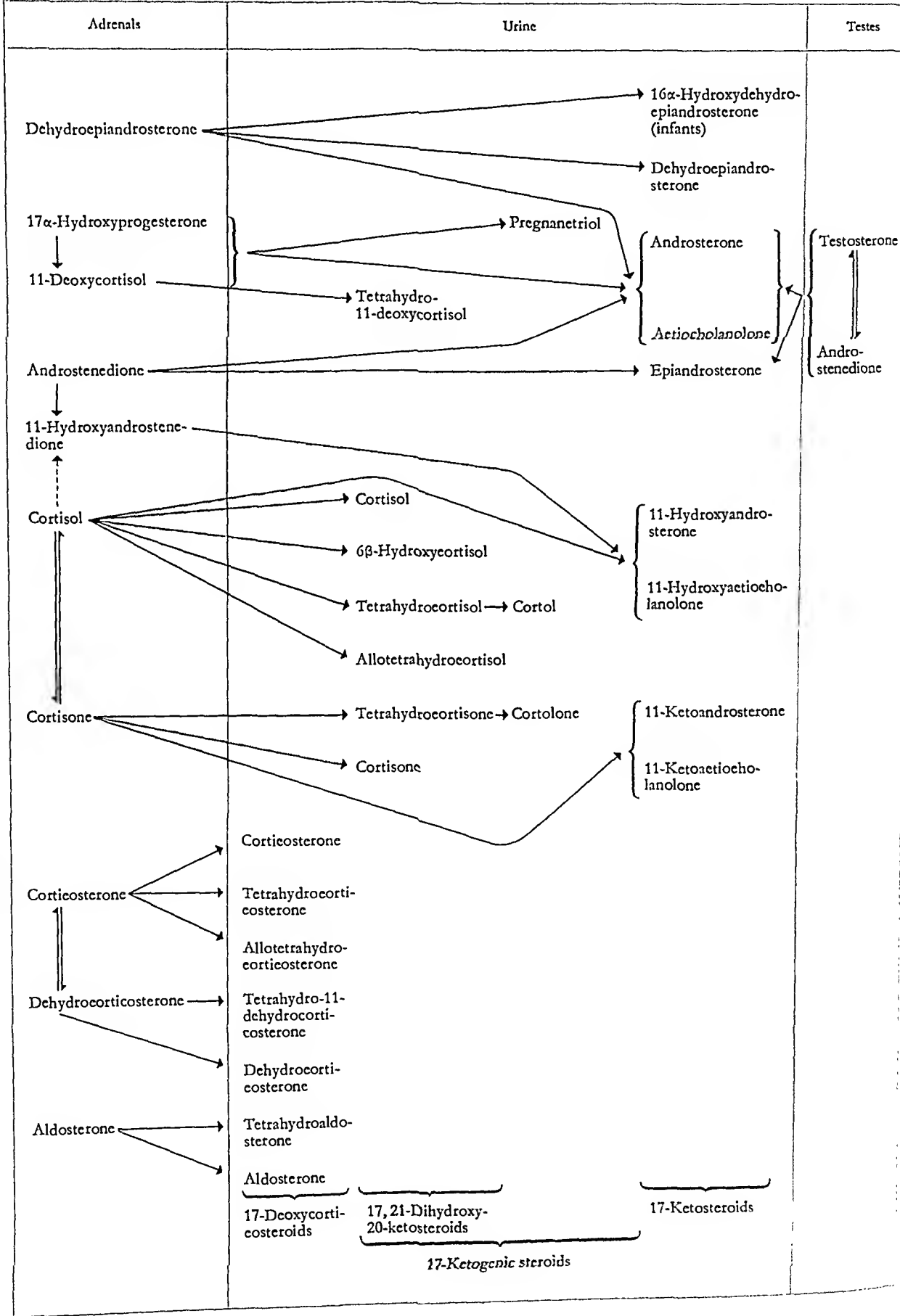
95-97% of the cortisol in the plasma is bound to a protein - probably an α-globulin - known as 'corticosteroid-binding globulin' or 'transcortin'.²² This protein binds cortisol more strongly



17-Hydroxycorticosteroid content of the plasma of 5 adults during the course of the day²⁵



Relationship of important urinary steroid fractions to the steroids of the adrenal cortex and testes



Urinary excretion of corticosteroids
(values for adults unless otherwise stated)

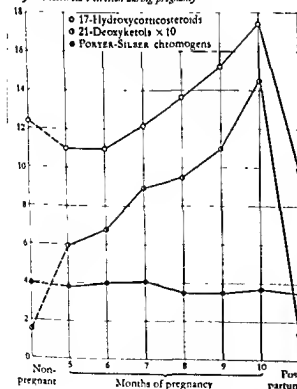
aldosterone is excreted mainly unchanged. Almost all the metabolites appear in the conjugated form as glucuronides or sul-
es. For a further discussion of corticosteroid metabolism see
428-430

the scheme opposite. There are differences of opinion as to which
the usual corticosteroid fractions determined in urine - the

urinary excretion of cortisol⁹⁷, cortisone⁹⁷ and aldosterone⁹⁹ in children and
11

	Cortisol		Cortisone		Aldosterone	
	μg/24h	μg/ 24h/kg body weight	μg/24h	μg/ 24h/kg body weight	μg/24h	μg/ 24h/kg body weight
Up to 1 year	1.0	0.11	6.9	0.86	2.1	0.24
1-5 years	3.9	0.23	14.4	0.85	3.5	0.23
5-10 years	7.3	0.26	23.9	0.76	4.9	0.17
11-15 years	14.4	0.29	35.2	0.71	6.5	0.13
16-20 years	20.6	0.33	47.2	0.76	6.6	0.10
21-30 years	31.3	0.42	63.7	0.89	7.5	0.10

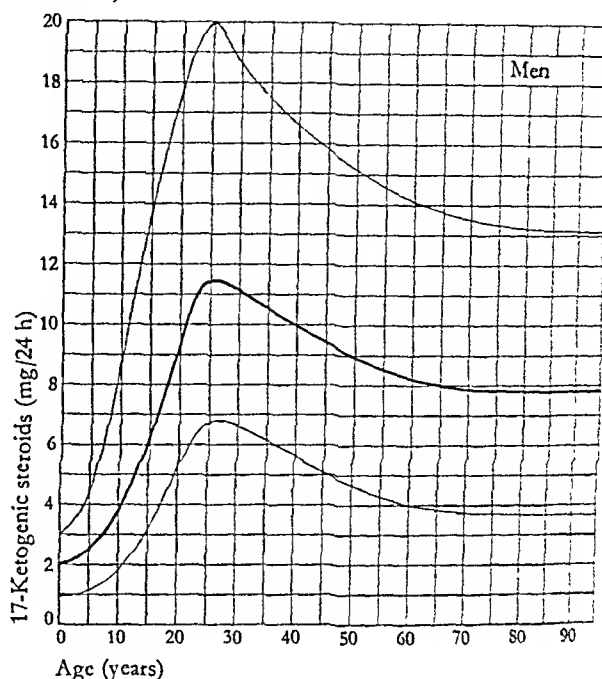
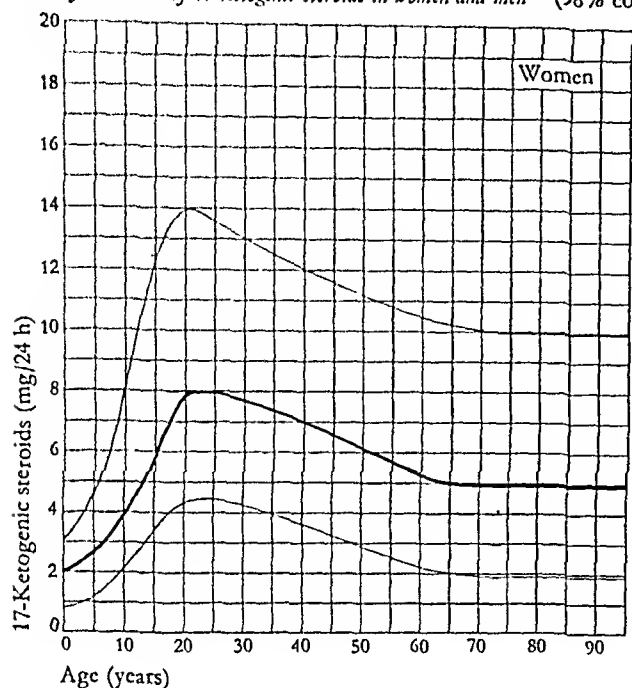
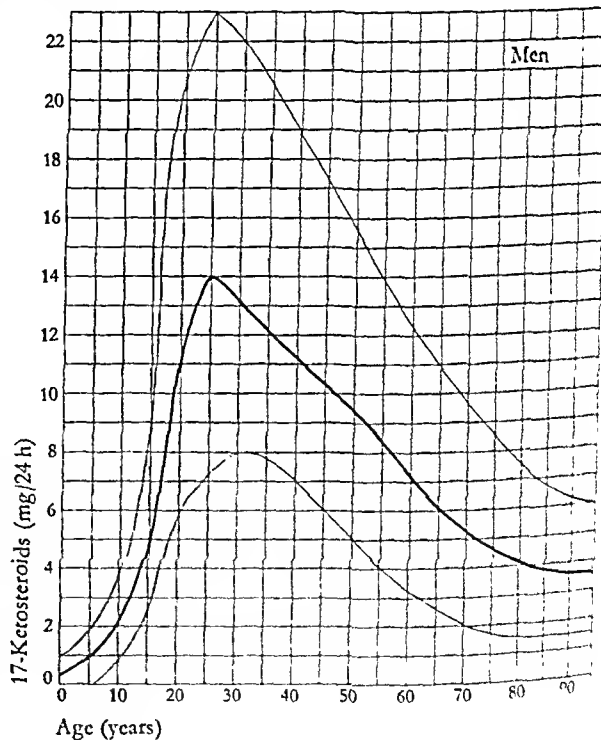
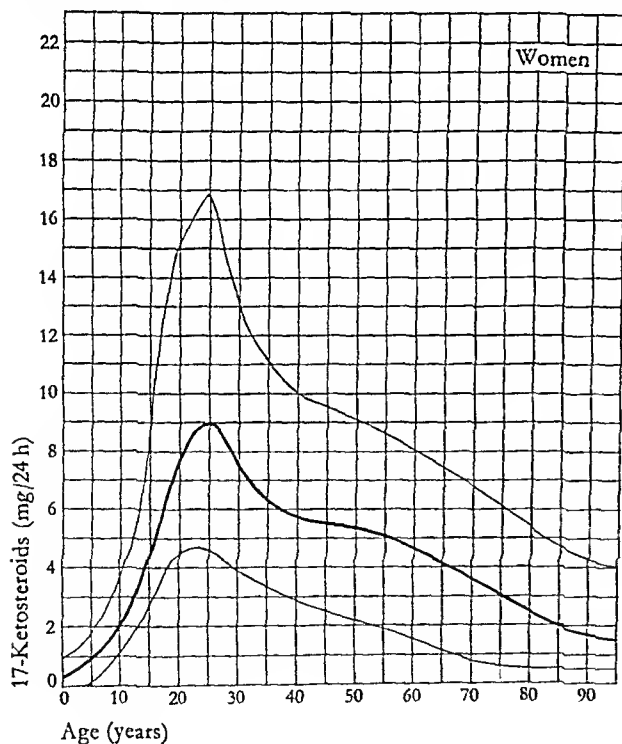
Urinary corticosteroid excretion during pregnancy²⁰



	Mean	Range	Reference
<i>Aldosterone</i> (μg/24 h)	5	2-10	⁹⁷
<i>Aldosterone, free</i> (μg/24 h)			
Newborn	-	0.03-0.13	⁹⁸
Adults	-	0.17-0.63	⁹⁸
<i>18-Aldosterone glucuronids</i> (μg/24 h) ..			
Newborn	-	0.4-2.5	⁹⁸
Adults	5.6	3.0-12.0	⁹⁸
<i>Corticosterons</i> (mg/24 h)	0.02	0-0.04	⁹⁷
<i>Cortisol</i> (mg/24 h)	0.07	0.03-0.09	⁹⁷
<i>Cortisol, free</i> (mg/24 h)	0.019	-	¹⁰⁰
<i>Cortisol glucuronids</i> (mg/24 h)	0.025	-	¹⁰⁰
<i>Cortisone</i> (mg/24 h)	0.09	0.06-0.14	⁹⁷
<i>Cortisone, free</i> (mg/24 h)	0.057	-	¹⁰⁰
<i>Cortisone glucuronids</i> (mg/24 h) ..	0.063	-	¹⁰⁰
<i>Cortisols</i> (mg/24 h)			
Men	1.9	0.3-2.9	⁹⁸
Women	1.1	0.5-1.6	⁹⁸
<i>11-Dehydrocorticosterons</i> (mg/24 h) ..	0.01	0-0.03	⁹⁷
<i>6α-Hydroxycortisol</i> (mg/24 h)			
Men	0.44	-	⁹⁸
Women	0.37	-	⁹⁸
<i>16-Hydroxydehydrocorticosterone</i> (mg/24 h)			
Newborn, up to 7 days	0.29	0.0-1.1	¹⁰¹
Infants, 4-6 months	0.04	0.0-0.16	¹⁰¹
<i>16-Hydroxypregnenolons</i> (mg/24 h)			
Newborn, up to 7 days	0.98	0.05-3.6	¹⁰¹
Infants, 4-6 months	0.02	0.0-0.08	¹⁰¹
<i>Pregnasterone</i> (mg/24 h)			
Children before puberty	-	<0.1	¹⁰²
Men	-	0.11-0.97	¹⁰³
Women	-	0.11-0.45	¹⁰³
<i>Tetrahydroaldosterons</i> (μg/24 h)			
Newborn	-	1.9-7.2	⁹⁸
Adults	-	40-60	⁹⁸
<i>Tetrahydrocorticosterons</i> (mg/24 h) ..	0.20	0.10-0.36	⁹⁷
<i>allo-Tetrahydrocorticosterons</i> (mg/24 h)	0.20	0.08-0.36	⁹⁷
<i>Tetrahydrocortisol</i> (mg/24 h)	1.0	0.6-1.6	⁹⁷
Men	2.2	0.8-2.8	⁹⁸
Women	1.9	0.5-3.7	⁹⁸
<i>allo-Tetrahydrocortisol</i> (mg/24 h)	0.4	0.1-0.7	⁹⁷
Men	1.1	0-2.8	⁹⁸
<i>Tetrahydrocortisone</i> (mg/24 h)	2.7	1.0-3.8	⁹⁷
<i>Tetrahydro-11-dehydrocorticosterone</i> ...	0.16	0.06-0.24	⁹⁷
<i>Tetrahydro-11-deoxycortisol</i> (mg/24 h) ..	0.06	0.02-0.10	⁹⁷

Corticosteroids

(For references see pages 750-751)

Urinary excretion of 17-ketogenic steroids in women and men²⁹ (98% confidence limits)Urinary excretion of 17-ketosteroids in women and men³¹ (mean and 98% confidence limits)

17-ketosteroids, the 17-ketogenic steroids or the 11-hydroxycorticosteroids – best represents the corticosteroid production of the adrenals^{32, 33, 39}. In men, about two-thirds of the total 17-ketosteroids are corticosteroid metabolites, one-third testicular steroid metabolites; in women they arise mainly from the corticosteroids, with a small contribution from the ovaries.

In assessing the significance of the urinary aldosterone excretion the state of hydration of the body as well as the potassium and sodium balance must be taken into account. The urinary pregnanetriol level is a valuable indication in patients with congenital adrenocortical hyperplasia. 16 α -Hydroxypregnenolone and 16 α -hydroxydehydroepiandrosterone – both steroids of adrenal origin – have

been found only in the urine of the newborn and infants; they are probably precursors of the oestrogens formed by the placenta.

Functional tests

The functional capacity of the adrenal cortex is determined by assaying the corticosteroids in the blood or urine after an exogenous dose of ACTH, usually 25–50 IU given intravenously^{32, 39}. More recently, the synthetic polypeptide tetracosactrin (31–41-corticotropin) has also been used for this purpose³⁴: in 66 subjects given an intramuscular dose of 0.25 mg the plasma level of 11-hydroxycorticosteroids rose from 147 μ g/l to 314 μ g/l within 30 minutes.

excretion of 17-ketosteroids in children and adults (mg/24 h)

	Number	11-Hydroxy- aetiocholanolone		11-Hydroxy- androsterone		11 Keto- aetiocholanolone		Dehydroepi- androsterone		Aetiocho- lanolone		Androsterone		Reference
		Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	
Boys, 3-12 years....	9	0.35	0.03-0.88	0.45	0.09-0.92	0.34	0.03-0.62	0.10	<0.01-0.33	0.35	0.04-0.82	0.32	0.07-0.82	104
Girls, 3-11 years ..	14	0.25	0.01-0.73	0.64	0.10-1.74	0.33	0.03-0.84	0.08	<0.01-0.34	0.50	0.01-1.56	0.67	0.01-2.28	104
Men, 19-43 years ..	10	0.6	0.3-1.1	1.6	1.0-2.1	0.6	0.3-1.4	2.3	0.8-6.4	2.8	1.4-5.1	3.4	1.5-6.0	104
Women, 18-43 years	25	0.6	0.2-1.2	1.4	0.2-2.9	0.7	0.2-1.4	1.1	0.1-2.6	2.7	0.7-4.3	3.1	0.9-4.8	104
Men, 50-71 years ..	11	0.8	0.2-2.2	1.7	0.8-3.1	0.7	0.2-1.5	0.7	<0.1-4.0	2.5	1.1-5.0	1.8	1.0-3.8	104
Women, 46-70 years	21	0.6	0.2-1.5	1.0	0.5-1.9	0.7	0.3-1.4	0.3	<0.1-0.7	2.2	0.9-3.7	1.3	0.5-3.8	104
Men,	8	0.7	0.3-1.6	0.6	0.3-1.0	0.7	0.2-1.1	0.6	0.1-1.4	2.1	1.0-3.1	2.1	1.1-3.5	105
Women	8	0.9	0.6-1.9	0.5	0.1-0.9	0.5	0.2-0.7	0.4	0.1-1.1	1.9	1.3-3.9	1.6	0.3-3.6	105

Diseases of the adrenal cortex can be identified by means of steroid suppression tests. These depend on the fact that cortisol secretion by the adrenal cortex - so long as it is dependent on the pituitary ACTH - can be suppressed by exogenous doses of corticosteroids. A test of this kind using oral doses of dexamethasone has been standardized by LIDDLE.³⁵ The metyrapone test is described on page 717.

Unlike the chemical assay of corticosteroids in body fluids, indirect functional tests are not of great diagnostic value. The commonest are the eosinophil test (TIRON's test)³⁶, the diuresis test³⁷ and tests involving studies of the electrolyte balance.

As shown in the table below there are also species differences in the activity of the corticosteroids, this is particularly marked between rats and man.⁴⁰

On the basis of their activity spectra the corticosteroids are often classified into mineralo- and glucocorticosteroids. A strict classification in this way is, however, impossible since the activity spectra overlap. Corticosteroids with an oxygen atom at C-11 mainly have an effect on carbohydrate and protein metabolism. The action of corticosteroids on mineral metabolism is essential for the maintenance of life, and death ensuing after complete failure of the adrenal cortex is usually attributed to this.

Action on carbohydrate and protein metabolism⁴¹ In animals that have been adrenalectomized, starvation leads to rapid depletion of the carbohydrate reserves, with lowering of the blood sugar level and glycogen content of the liver and muscles. Adrenalectomized animals are also hypersensitive to exogenous insulin. Similar disturbances of carbohydrate metabolism occur in patients with Addison's disease. Administration of corticosteroids reverses these changes. Corticosteroids cause a rise in both nitrogen excretion and the amino-acid content of the blood, whence it can be concluded that they cause a breakdown of protein.

with a reduced response to insulin.

This catabolic action of the corticosteroids is reflected in tissue breakdown, diminution of the muscle mass, osteoporosis and thinning of the epidermis. The mechanism of these processes has been only partially elucidated.

Corticosteroids also have an effect, both *in vivo* and *in vitro*, on the activity of many enzymes.⁴² Thus in the liver they increase the activity of glucose-6-phosphatase and enzymes, like tryptophan oxygenase and tyrosine aminotransferase, involved in amino-acid

metabolism. At the same time corticosteroids promote the formation of messenger-RNA and the *de novo* synthesis of enzymes.^{42,43} Possibly this activity derives from a direct effect of corticosteroids on gene activity.⁴⁴

Renal function is reflected in changes in electrolyte and water balance. Hypofunctioning of the gland results in loss of sodium in

have markedly greater effects on mineral metabolism than cortisol. Both aldosterone and deoxycorticosterone augment the reabsorption of sodium in the distal renal tubules and at the same time promote potassium excretion, while the resulting sodium retention results also in water retention. Aldosterone most likely acts by promoting active sodium transport, as has been demonstrated in the urinary bladder of the toad.⁴⁵ The first event is possibly a direct involvement of aldosterone in the nuclear synthesis of messenger RNA.⁴⁶

Cortisol acts in a different way. Like aldosterone, but to a lesser extent, it promotes sodium reabsorption in the distal tubules, but

Relative activity of corticosteroids in adrenalectomized animals⁴⁷

	Decrease urinary Na ⁺ /K ⁺ ratio (rats)	Growth and survival (rats)	Survival (dogs)	Muscle- work test (rats)	Glyco- gen de- position (rats)
Cortisone	0.6	2.5	0.5	10	10
Cortisol	0.8	3	-	19	16
Deoxycorticosterone	1.4	1	-	-	5
11-Dehydro- corticosterone	-	10	-	5	5
11-Deoxycortisol	0.8	-	-	0.2	-
11-Deoxycortico- sterone	10	10	10	0.2	0.1
Aldosterone	1000	-	250	-	3

the increased potassium excretion seems more likely to be due to mobilization of tissue potassium than to an effect on renal function. The lowered diuresis occurring in adrenocortical insufficiency can be corrected by giving cortisol but not aldosterone. Cortisol appears to be necessary for maintenance of tubular function and thus of normal diuresis.

Action on blood circulation. This is mainly secondary to the action on water and electrolyte balance (reduction of plasma volume and increase in blood viscosity in adrenocortical insufficiency) but the corticosteroids also have a direct effect on the capillaries, arterioles and myocardium. The stimulating effect of corticosteroids on adrenaline release is also reflected in circulatory changes.

Action on muscles. The impairment of muscular function in adrenocortical insufficiency is primarily a result of the reduced circulation. In primary aldosteronism muscle weakness is due to the lowered blood potassium level, in CUSHING's syndrome to the increased breakdown of muscle.

Action on the central nervous system. The corticosteroids affect the excitability of the brain and the emotions. This is mainly a result of the action of these substances on the cerebral circulation and on the metabolism of γ -aminobutyric acid and electrolytes in the brain⁴⁸.

Action on lymphatic tissues. Exogenous corticosteroids give rise to marked involution of the lymphatic organs, with involvement of both the parenchymal and reticular connective-tissue cells⁴⁹. In the initial phase there is characteristic breakdown of the thymocytes in the thymus and of the lymphocytes in the lymph glands and to a lesser extent in the spleen. Following this lymphocytolysis is a second phase marked by inhibition of new cell formation on the one hand (manifested by the absence of mitosis in the thymus, lymph glands and spleen) and by degeneration of the reticular connective tissue on the other.

Corticosteroids cause both an increase and decrease in the numbers of circulating antibodies; the mechanism of these effects is still largely obscure. In man, as in monkeys and guinea-pigs, corticosteroids seem to have little effect on antibody formation, but in rabbits, rats and mice antibodies may be suppressed by these substances under certain conditions.

Action on eosinophils. Administration of corticosteroids or ACTH reduces the number of circulating eosinophils, an effect utilized in THORN's test for adrenocortical insufficiency. The mechanism is unknown⁵⁰.

Anti-inflammatory action. Administration of glucocorticoids inhibits or suppresses most inflammatory processes of a toxic, allergic, infectious or traumatic nature. Their effect is, however, merely palliative, and the symptoms reappear when the steroids are withdrawn⁵¹. This action has been ascribed to a protective effect of corticosteroids on the lysosomal membranes⁵², the liberation of whose protein-splitting enzymes is thought to cause inflammation.

Action on the pituitary. The circulating corticosteroids exert an inhibitory action on pituitary secretion of ACTH (for further discussion see page 717).

Synthetic steroids. Chemical modification of the steroid skeleton has resulted in synthetic compounds of greater physiological activity and higher specificity than the natural corticosteroids. Over

1200 biologically active steroids, natural and synthetic, are known. In the table on this page the effects of some synthetic steroids are compared with those of cortisone and cortisol.

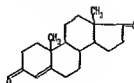
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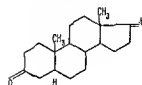
Physiological activity of natural and synthetic steroids⁵³

	Anti-inflammatory activity	Sodium retention	Potassium excretion	Effect on carbohydrate metabolism
Cortisone	1	1	1	1
Cortisol	1-1.25	1-1.25	1	1.25
Prednisone	3-5	slight	slight	3-5
(1-dehydrocortisone)				
Prednisolone	3-5	slight	slight	3-5
(1-dehydrocortisol)				
6 α -Methylprednisolone ...	3-5	none	slight	3-5
9 α -Fluorocortisol	10-15	300-900	10-25	10-25
Triamcinolone	3-5	none	slight	3-5
(9 α -fluoro-16 α -hydroxy-prednisolone)				
Dexamethasone	15-28	none	slight	30
(9 α -fluoro-16 α -methyl-prednisolone)				

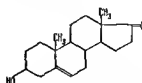
Androstenedione



Androstanedione



Dehydroepiandrosterone



Steroids with androgenic activity have also been synthesized, for example 17-methyltestosterone and fluoxymesterone². Synyl long-chain esters of testosterone (testosterone cypionate, testosterone enanthate, testosterone phenylacetate) show prolonged androgenic activity. Other testosterone derivatives with an anal but less actively virilizing effect have been synthesized, for example methandrostenolone, 19-nortestosterone, norethandrolone⁴.

Unit

0.1 mg androsterone.

Methods of assay²

Androgenic activity can be measured biologically on birds (see

Biosynthesis, secretion, metabolism²

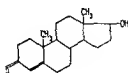
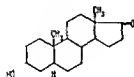
Testosterone is secreted by the adrenal cortex in amounts of 0.05-0.1 mg, the corresponding amounts for the adrenal cortex being 2-3 mg 9-10 mg respectively¹⁰ (see also page 743). Androstenedione

Androgens^{1, 2} (for references see page 753)

Chemistry

The androgens comprise a group of steroids the administration of which compensates for the effects of castration in the adult male animal and promotes the development of the male accessory reproductive glands and secondary sexual characteristics in the sexually immature animal.

Testosterone

Androsterone
(androstan-3 α -ol-17-one)

Leydig cells appears to be stimulated only by the gonadotropin (HCG)^{10, 11} whereas adrenocortical synthesis

Production rates of androgens (mg/24 h)

	Mean	Range	s	Reference
Testosterone				
Men.....	7	—	—	24
Women.....	0.34	—	—	24
Men.....	—	3.58–7.56	—	25
Women.....	—	0.42–0.94	—	25
Men.....	6.8	—	—	26
Women.....	0.23	0.13–0.33	0.073	27
Androstenedione				
Men.....	1.4	—	—	24
Women.....	3.4	—	—	24
Women.....	3.3	1.7–6.3	1.86	27
Epitestosterone				
Men.....	0.22	—	—	26

Androgens in plasma

	Mean	Range	s	Reference
Testosterone (µg/l)				
Men.....	8.0	5–11	2.5	33
Women.....	0.69	—	—	33
Men.....	6.4	3.2–13.0	2.0	34
Women.....	0.36	0.13–0.80	0.09	34
Women.....	0.37	0.20–0.70	0.09	35
Pregnancy				
20–31 weeks.....	3.8	3.0–4.6	—	14
39–42 weeks.....	9.0	5.9–11.7	—	14
Androstenedione (µg/l)				
Adolescents.....	0.50	—	—	36
Men.....	0.60	—	0.12	37
Women.....	1.40	—	0.32	37
Women.....	1.67	0.9–2.1	0.40	35
Dehydroepiandrosterone sulphate (mg/l)				
Men.....	1.5	—	—	30
Women.....	1.0	—	—	30
Androsterone sulphate (mg/l)				
	0.4	—	—	30

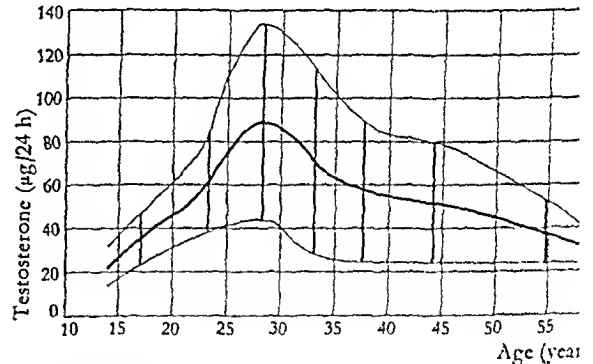
on testicular function in men¹⁰ and on virilizing processes and pathic hirsutism in women².

Testosterone injected into the blood stream is rapidly broken down, the half-life being about 4 min¹⁶. The most important breakdown products of testosterone and androstenedione are androsterone and aetiocholanolone (see page 746), the excretion of which is discussed in connection with the 17-ketosteroids in the section on 'Corticosteroids', page 749. In urine, testosterone is present only as the glucuronide, dehydroepiandrosterone mainly as the sulphate. Published data on the urinary excretion of testosterone are conflicting, but recent values from which the variation which can be seen are shown in the table and figure on this page. Like plasma level, the urinary excretion of testosterone in women varies during the course of the menstrual cycle^{18,19}, with a maximum during and immediately following menstruation and a minimum during the luteal phase of the cycle. The urinary testosterone excretion may fall after the menopause¹⁹.

Urinary testosterone excretion (µg/24 h)

	Mean	Range	s
Testosterone, total			
Children, < 10 years.....	0.4	0.1–0.8	—
Men.....	37	20–65	—
Women.....	7.7	3–14	—
Men, 16–20 years.....	78	60–103	—
Men, 21–63 years.....	51.7	40–65	—
Women, 20–55 years.....	6.5	2.1–10.7	—
Testosterone glucuronide			
Men.....	72	33–120	—
Women.....	12	7–18	—
Testosterone sulphate			
Men.....	—	~5–10	—
Testosterone, free			
Men.....	1.1	—	—
Women.....	0.7	—	—
Epitestosterone glucuronide			
Men.....	182	—	—
Women.....	36	—	—

Testosterone excretion in normal men (mean $\pm 2 \times$ standard deviation 68 subjects)¹⁷



Biological activity

Testosterone has an anabolic effect on protein metabolism² and this hormone and its synthetic derivatives have been shown to promote nitrogen retention and accelerate the recovery of persons suffering from nutritional protein deficiency. Testosterone has more marked effects on boys before puberty and on women than on men. The site of action of the hormone in protein synthesis is probably the transfer of the s-RNA/amino acid complex to the ribosomes.

Comparative activities of androgens¹

	Capon comb test	Seminal vesicle test (rats)	Virilizing effect (women)
Testosterone.....	100	100	100
Androsterone.....	10	10	—
Androstenedione.....	12	20	<5
Androstanedione.....	12	14	—
Dehydroepiandrosterone.....	16	3	<5
Methyltestosterone.....	60	—	—

Synthetic progestational steroids are mostly derived from 17 α -acetoxyprogesterone². In addition to their progestational effect, derivatives of 19-nortestosterone have a marked androgenic action².

Methods of assay

Biological³. For clinical purposes biological tests are either not sensitive enough or are cumbersome. In the laboratory's test, the Δ^4 -pregnen-20-one is converted to Δ^4 -pregnen-20-one-3 α -ol-20-one by the action of 3 α -HSD. The reaction is measured by the formation of a semicarbazone at 280 nm⁶. Fluorimetric, colorimetric and more recently gas-chromatographic and double isotope dilution techniques are also available. Pregnenediol is best determined colorimetrically, for instance by the method of KLOPPER et al⁶, or by gas chromatography.

Biosynthesis, secretion, metabolism^{7,8}

Progesterone is an intermediary metabolite in the biosynthesis of all other steroid hormones, and is secreted by the adrenal cortex, ovaries, testes and placenta. The corpus luteum of the ovaries and the placenta are the quantitatively most important sources. The amount contained in these organs (corpus luteum ca 20 μ g/g⁹, placenta 2-4 μ g/g¹⁰) is small in comparison with the amount secreted.

Progesterone production remains roughly proportional to the weight of the placenta, at term it is about 250 mg per day¹¹.

Production rates of progesterone and pregnenolone* (mg/24 h)

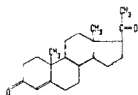
	Mean	Range	Reference
Progesterone			
Men	-	1.1-6.5	28
Men, 23-34 years	5.1	3.2-7.4	29
Men, 74-79 years	1.5	0.8-1.9	28
Women, ovariectomized	-	0.9-2.5	28
Women, proliferation phase	-	2.5-5.4	28
Women, luteal phase	-	22-43	29
Pregnenolone			
Men, 23-34 years	15	9-22	29
Men, 74-79 years	3.5	2.6-5.1	29

* Urinary production rates (obtained from urinary excretion of pregnenediol)

Plasma levels of progesterone and some of its metabolites are

to albumin¹². In the fetus, progesterone is converted to plasma proteins, principally

Metabolism. Injected progesterone disappears in 11 h.



Plasma levels of progesterone and its metabolites ($\mu\text{g/l}$)

	Mean	Range	s	Reference
Progesterone				
Women, proliferative phase.....	—	0–5.3	—	31
Women, luteal phase ...	—	6–21	—	31
Women, proliferative phase.....	1.13	—	0.49	32
Women, luteal phase ...	10.4	—	3.2	32
Women, ovariectomized	0.39	—	0.10	32
Men.....	0.28	—	0.13	32
Men.....	0.28	<0.15–0.48	—	33
Umbilical vein	372	—	60	34
Umbilical artery.....	140	—	18	34
17α-Hydroxyprogesterone				
Women, proliferative phase.....	0.42	—	0.20	27
Women, luteal phase ...	1.74	—	0.46	27
Men.....	0.95	—	0.31	27
Umbilical vein.....	6	—	—	34
Umbilical artery.....	33	—	—	34
20α-Hydroxypregnenone				
Umbilical vein.....	10	—	—	34
Umbilical artery.....	27	—	—	34
20β-Hydroxypregnenone				
Umbilical vein.....	3	—	—	34
Umbilical artery.....	14	—	—	34
Pregnanediol				
Women.....	—	65–129	—	35

Urinary excretion of progesterone metabolites (mg/24 h)

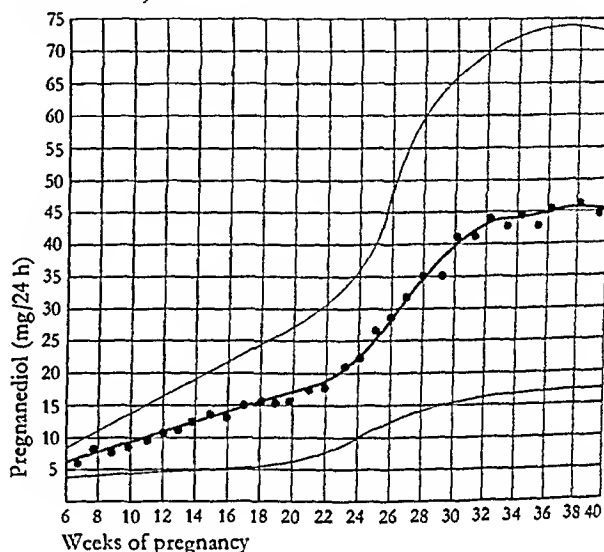
	Mean	Range	s	Reference
Pregnanediol				
Boys, 3–15 years	0.76	—	0.32	36
Girls, 3–15 years	0.72	—	0.60	36
Men.....	0.92	0.38–1.42	—	6
Women, proliferative phase.....	1.12	0.78–1.50	—	6
Women, luteal phase ...	3.3	2.1–4.2	—	6
Women, postmenopausal	0.63	0.28–0.86	—	6
Women, proliferative phase.....	0.48	0.10–1.26	0.31	37
Women, luteal phase ...	2.68	1.17–9.50	1.68	37
Men, 23–34 years	0.6	—	0.17	29
Men, 74–79 years	0.15	—	0.07	29
Pregnanolone				
Men.....	—	0.14–0.60	—	38
Women.....	—	0.06–0.46	—	38

70% of injected progesterone can be recovered from urine and faeces, and less than 40% can be accounted for as known metabolites⁷.

During the proliferation phase of the menstrual cycle pregnanediol excretion is usually less than 1 mg/24 h; this pregnanediol

probably originates mainly from the steroids formed in the adrenal cortex. After ovulation, pregnanediol excretion increases and in the luteal phase usually reaches 2–6 mg/24 h. In this phase the greater part of the pregnanediol arises from progesterone secreted by the corpus luteum. A few days before menstruation pregnanediol excretion begins to fall, reaching a minimum 2 or 3 days after the start of the period.

The progesterone formed in the placenta passes into the foetus, where it is broken down into less active compounds like 17 α -hydroxyprogesterone and the 20 α - and 20 β -hydroxypregnenones. There is a dynamic exchange of progesterone and its metabolites between foetus and placenta, mother and placenta, and foetus and mother¹⁷. During pregnancy, the excretion of pregnanediol increases (see the diagram below), as does that of pregnanolone¹⁹; after parturition it falls again, reaching the proliferation phase value in about a week²⁰. Pregnanediol has been isolated from the meconium, where it is present to the extent of 85–95% as sulphate²¹.

Urinary pregnanediol excretion during pregnancy¹⁸ (mean and 95% confidence limits)

Regulation of progesterone secretion. Little is known of the manner in which progesterone synthesis and secretion is regulated^{2,7,22,23}. The formation of the hormone in the ripening follicle is probably stimulated only by LH; whether its secretion during the luteal phase is stimulated by prolactin as well as LH is not known for certain. The manner in which progesterone formation in the placenta is regulated has not been explained, but HCG may play a role in this. Under certain conditions, HCG has been observed to increase progesterone secretion in the corpus luteum.

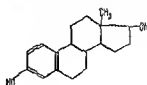
Biological activity

The main action of progesterone is the maintenance of pregnancy²⁴, the mechanism of which is poorly understood²⁵, though it is known that progesterone blocks the spread of the uterine contractile response to oxytocin²⁴. The hormone also has other effects on the uterus, notably on its composition and metabolic activity; thus it causes an increase not only of uterine weight but of the collagen, nucleic acid, glycogen and lipid contents of the organ. In many of its uterine effects progesterone acts only in conjunction with oestrogens⁷.

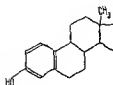
The biological activity of progesterone is not confined to the reproductive cycle. The hormone has an inhibitory effect in vitro on enzymes of the respiratory chain and stimulates the metabolism of galactose⁷. It is antagonistic to the sodium-retaining effects of aldosterone and deoxycorticosterone but does not affect potassium excretion; progesterone administration is followed by a compensatory increase in aldosterone secretion. Progesterone has a catabolic effect and causes increased urinary nitrogen excretion; there is some evidence that this is due to inhibition of amino-acid utilization by the liver. In rats and mice, the hormone causes an increase in body weight due to deposition of fat. These general metabolic effects of progesterone probably have little physiological significance except when large amounts of the hormone are secreted.

Progesterone - Oestrogens

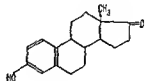
Oestradiol (17 β -oestradiol)



Oestrinol



Oestrone



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Methods of assay

Biological² For example, induction of the characteristic

physiol

Chemical³ Oestrogens can be determined colorimetrically

reaction) or fluorimetrically (reaction with the fol...

Biosynthesis, secretion, metabolism⁴

The biosynthesis of the oestrogens is summarized in

VAN DER MOLEN and GROEN, *J. clin. Endocr.*, 23, 1625 (1965)

ZANDER, J., in WOLSTENHOLME and CAMERON (Eds.), *Progesterone and the De-*
velopment of Pregnancy, Ciba Foundation Study Group, No 9, Churchill,

Oestrogens (for references see page 757)

Chemistry

All naturally occurring oestrogens are unsaturated phenolic

Chemical fraction

Oestrogenic activity is also seen in plant phenols such as coumestrol

Production rates of oestradiol (μ g/24 h)

	Mean	Range	n
Women, ...	—	200-500	—
Women, ...	—	93-165	—
Women, mid-cycle ...	—	up to 300	—
Women, start of cycle ...	—	35-100	—
Men, 21-37 years ...	70	—	29

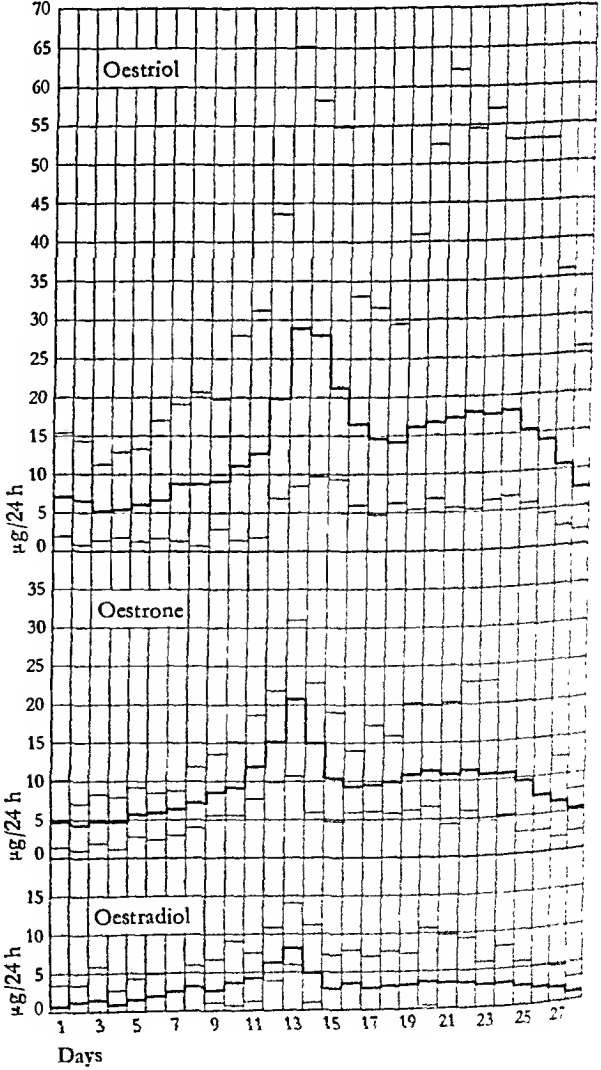
Oestrogens in plasma (µg/l)

	Mean	Range	s	Reference
<i>Women</i>				
Proliferative phase				
Oestriol.....	0.25	—	0.12	32
Oestrone.....	0.20	—	0.11	32
Oestradiol.....	0.13	—	0.08	32
Ovulation				
Oestriol.....	0.37	—	0.23	32
Oestrone.....	0.70	—	0.25	32
Oestradiol.....	0.28	—	0.17	32
<i>Men</i>				
Oestrone.....	0.42	—	0.09	33
Oestradiol.....	0.15	—	0.12	33
Oestriol.....	—	trace	—	34
<i>Pregnancy</i>				
36th–38th week				
Oestrone + oestradiol ...	92	—	32	35
Oestriol.....	81	—	35	35
39th–42nd week				
Oestrone + oestradiol ...	108	—	37	35
Oestriol.....	93	—	39	35
At term				
Oestriol.....	—	43–175	—	36
Oestrone.....	—	27–103	—	36
Oestradiol.....	—	13–29	—	36
<i>Cord blood</i>				
Oestriol.....	583	—	—	37
Oestrone.....	13	—	—	37
Oestradiol.....	6	—	—	37

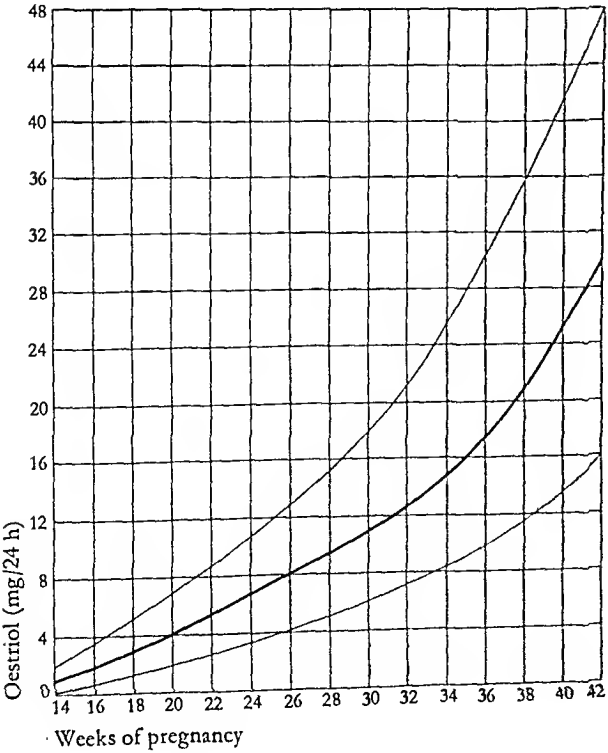
Urinary excretion of oestrogens (µg/24 h)

	Mean	Range	Reference
<i>Children, 9–12 years</i>			
Total oestrogens.....	—	<1.0	38
<i>Women, postmenopausal</i>			
Total oestrogens.....	5.5	3.2–9.0	20
Oestriol.....	3.9	2.2–7.5	20
Oestrone.....	1.3	0.3–2.4	20
Oestradiol.....	0.3	0–1.4	20
<i>Men, 20–50 years</i>			
Total oestrogens.....	10.3	6.0–17.8	39
Oestriol.....	3.5	0.8–11.0	39
Oestrone.....	5.4	3.0–8.2	39
Oestradiol.....	1.5	0–6.3	39
<i>Pregnancy, 1 week ante partum</i>			
Total oestrogens.....	30 800	23 200–37 200	40
Oestriol.....	29 000	22 000–35 000	40
Oestrone.....	1 400	930–1 600	40
Oestradiol.....	520	380–630	40

Urinary oestrogen excretion during the menstrual cycle²⁰ (mean and highest and lowest values in 16 women aged 18 to 41 years)



Urinary oestriol excretion during pregnancy¹⁹ (mean and 95% range)



Foetus, placenta and mother appear to be separate compartments in this respect, and not all oestrogens and oestrogen metabolites

Normal plasma oestrogen levels are given in the table opposite the course of the menstrual cycle the highest values occur shortly

oid hormones, the oestrogens are the most strongly bound to plasma proteins¹⁴

Many oestrogen metabolites are 16-epioestrinol, 16 α -hydroxyestrone, 16-keto-oestradiol, 16 β -hydroxyoestrone, 2-methoxyoestrone and 2-methoxyoestrinol¹⁶, as well as 15 α -hydroxyoestrone, β -hydroxyoestrone and 15 β -hydroxyoestradiol-17 β ¹⁷. The urinary oestrogens are conjugated almost exclusively with glucuronic

References

¹ EAGLESON and MARSHALL (DORFMAN, R. I. (Ed.), *Methods in Hormone Research*, vol. 3, Academic Press, New York, 1967, p. 1.

² PETERSON and GILBERT (J. Endocrinol. Monographs, Cambridge, 1967).

³ LUTTEN et al., *Biochem. J.*, **96**, 33C (1965); KUFFEN et al., *Steroids*, **8**, 403 (1966).

⁴ BRIDE et al., *J. clin. Endocr.*, **22**, 935 (1962).

⁵ MOORE et al., *J. Endocr.*, **26**, 25 (1963).

⁶ GOERING et al., *Amer. J. Obstet. Gynec.*, **92**, 441 (1965); GOERING and HERRMANN, *J. clin. Endocr.*, **26**, 65 (1966).

Regulation of oestrogen secretion¹⁷ Both FSH and LH appear to be necessary for oestrogen formation. The synthesis is also stimulated in men and women by HCG.

Biological activity

The oestrogens have a similar but weaker anabolic action on protein metabolism and cause retention of sodium and water

Functions of the sex hormones

	Androgens	Oestrogens	Progesterone
<i>Male organism</i>			
Development of primary sex organs:			
General, especially testes, prostate, penis.....	+++	Antagonist	
Muscles and connective tissue of accessory glands.....	?	+	
Development of secondary sex characteristics.....	++++	Antagonist	
Emotional behaviour: libido, masculine activity.....	++++	Antagonist	
<i>Female organism</i>			
Development of primary sex organs.....	Partial antagonist	+++	0
Development of secondary sex characteristics.....	Antagonist	++++	?
Emotional behaviour:			
Frigidity.....	Antagonist	++++	+
Libido.....	+++	+	Partial antagonist
<i>Menstrual cycle</i>			
Maturation of ovum.....	?	+++	+
Proliferation phase.....	?	++++	+
Secretion phase.....	?	+	++++
Migration of ovum, nidation.....	?	++	+++
<i>Pregnancy</i>			
Inhibition of maturation of further follicles; quiescence of the uterus; relaxation of the uterine muscles (1); lowering of the Na:K ratio in blood; lowering of the sympathetic tonus (2).....	?	{ Antagonist to (1); synergist to (2) }	++++
Indispensable for maintenance of pregnancy.....	?	++	++
Relaxation of the pelvic girdle; increase of tonus of uterine muscles towards end of pregnancy (3).....	?	+++	Antagonist to (3)
Growth of mammary tissue.....	?	++*	++*
Inhibition of lactation until parturition.....	?	++	+
<i>Post partum</i>			
Maintenance of lactation.....	?	++*	++*
Inhibition of lactation at high therapeutic dosage.....	++	+++++	0
Involution of the uterus and preparation for fresh menstrual cycle...	?	+++	0
* See also under 'Prolactin', page 719.			

International Biological Standards and Reference Preparations¹

Substance	International Unit (IU) mg	Form in which dispensed	Year of establishment
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Antigens I

Held by International Laboratory for Biological Standards, Statens Serum Institut, Copenhagen

Old tuberculin	(0.011 111 µl)	Ampoules containing 2 ml (90 000 IU per ml)	1965 (3rd Stat)
Mammalian tuberculin (purified protein derivative)	0.000 28	Ampoules containing 10 mg plus 4 mg of salts (500 000 IU per ampoule)	1951 (1st Stat)
Avian tuberculin (purified protein derivative)	0.000 072 6	Ampoules containing 10 mg plus 26.3 mg of salts (500 000 IU per ampoule)	1954 (1st Stat)
Tetanus toxoid (adsorbed, purified)	0.03	Ampoules containing 25 mg plus glycine (833 IU per ampoule)	1951 (1st Stat)
Tetanus toxoid (adsorbed)	0.666 7	Ampoules containing 80 mg adsorbed to aluminium hydroxide, plus an equal part of guinea-pig serum, dried (120 IU per ampoule)	1965 (1st Stat)
Diphtheria toxoid (adsorbed, purified)	0.50	Ampoules containing 50 mg plus glycine (100 IU per ampoule)	1951 (1st Stat)
Diphtheria toxoid (adsorbed)	0.75	Ampoules containing 80 mg adsorbed to aluminium hydroxide plus an equal part of guinea-pig serum, dried (107 IU per ampoule)	1955 (1st Stat)
Schick test toxin (diphtheria) (purified)	0.004 2	Ampoules containing 0.005 mg plus 1 mg of bovine albumin and 2.74 mg of phosphate buffer salts (900 IU per ampoule)	1954 (1st Stat)
Perussis vaccine (dried)	1.5	Ampoules containing 52 mg (34.7 IU per ampoule)	1957 (1st Stat)
Oral vaccine (Polio) (dried)	-	Ampoules containing 20 mg (1.6 x 10 ¹⁰ organisms per ampoule)	1953 (1st Ref Prepara)
Oral vaccine (Polio) (dried)	-	Ampoules containing 20 mg (1.6 x 10 ¹⁰ organisms per ampoule)	1953 (1st Ref Prepara)
Cardiolipin (purified)	-	Ampoules containing 4, 8 or 16 ml of a solution in ethanol (6.0 mg cardiolipin per ml as calculated from the phosphorus content)	1967 (4th Ref Prepara)
Lactin (beef heart, purified)	-	Bottles containing 30 ml of a solution in ethanol (30.3 mg lactin per ml)	1953 (2nd Ref Prepara)
Lactin (egg, purified)	-	Ampoules containing 4, 8 or 16 ml of a solution in ethanol (26.7 mg of lactin per ml as calculated from the phosphorus content)	1959 (3rd Ref Prepara)
Rabies vaccine	-	Ampoules containing 121 mg of a UV-inactivated, freeze-dried suspension of rabbit brain infected with fixed rabies virus	1965 (2nd Ref Prepara)
Smallpox vaccine (freeze-dried)	-	Ampoules containing 14 mg	1962 (1st Ref Prepara)
Typhoid vaccine (killed, emulsified, dried)	-	Ampoules containing 11 mg	1962 (1st Ref Prepara)
Typhoid vaccine (killed, emulsified, freeze-dried)	-	Ampoules containing 34 mg	1962 (1st Ref Prepara)
Poliovirus vaccine (killed, emulsified, freeze-dried)	-	Ampoules containing 10 ml	1962 (1st Ref Prepara)
BCG vaccine (dried)	-	Ampoules containing dried vaccine derived from 2.5 mg (wet dry weight) of bacillary mass of BCG and 5 mg of medium glutamate (total weight of dried material 5.72 mg per ampoule)	1965 (1st Ref Prepara)
Edwards virus (embryo cells) (purified, freeze-dried)	0.093 661	A = 0.111 111 µl B = 0.111 111 µl C = 0.111 111 µl D = 0.111 111 µl E = 0.111 111 µl F = 0.111 111 µl G = 0.111 111 µl H = 0.111 111 µl I = 0.111 111 µl J = 0.111 111 µl K = 0.111 111 µl L = 0.111 111 µl M = 0.111 111 µl N = 0.111 111 µl O = 0.111 111 µl P = 0.111 111 µl Q = 0.111 111 µl R = 0.111 111 µl S = 0.111 111 µl T = 0.111 111 µl U = 0.111 111 µl V = 0.111 111 µl W = 0.111 111 µl X = 0.111 111 µl Y = 0.111 111 µl Z = 0.111 111 µl	1967 (1st Ref Prepara)

Antigens II

Held by International Laboratory for Biological Standards, Central Veterinary Laboratory, Weybridge, England

Equine encephalomyelitis vaccine (killed, dried)	0.42	Ampoules containing 470 mg, derived from formalin-treated <i>Equine encephalomyelitis</i> (E. encephalomyelitis) type B, adsorbed to aluminium hydroxide (1 700 IU per ampoule)	1959 (1st Stat)
Newcastle disease vaccine (killed, emulsified, freeze-dried)	1.0	Ampoules containing 525 mg of vaccine derived from formaldehyde-treated allantoic fluid of eggs infected with virus of Newcastle disease virus adsorbed to aluminium hydroxide (525 IU per ampoule)	1963 (1st Stat)
Newcastle disease vaccine (killed, emulsified)	-	Ampoules containing 199.5 mg of allantoic fluid derived from eggs infected with the virus (Hitchner B ₁ strain)	1967 (1st Ref Prepara)
Canine distemper virus vaccine (killed, emulsified)	-	Ampoules containing 53.4 mg	1956 (1st Ref Prepara)

¹ From *W. H. O. Expert Committee on Biological Standards, 2nd H. 14 Org. Ind. Res. Ser.*, No. 413 (1957).

Substance	International Unit (IU) mg	Form in which dispensed	Year of establishment
Antibodies I			
Held by International Laboratory for Biological Standards, Statens Seruminstitut, Copenhagen			
Tetanus antitoxin (hyperimmune horse serum, dried)	0.309 4	Bottles containing 10 ml of a solution in saline, containing 66 vol% glycerol (5 IU per ml)	1928 (1st Standard)
Diphtheria antitoxin (hyperimmune horse serum, dried)	0.062 8	Bottles containing 10 ml of a solution in saline, containing 66 vol% glycerol (10 IU per ml)	1922 (1st Standard)
Antidysentery serum (S111GA) (hyperimmune horse serum, dried)	0.05	Bottles containing 10 ml of a solution in saline, containing 66 vol% glycerol (200 IU per ml)	1928 (1st Standard)
Gas-gangrene antitoxin (<i>perfringens</i>) (<i>Clostridium welchii</i> type A antitoxin; hyperimmune horse serum, dried)	0.334 6	Bottles containing 90.35 mg (270 IU per ampoule)	1963 (5th Standard)
Gas-gangrene antitoxin (<i>vibrio septique</i>) (hyperimmune horse serum, dried)	0.118	Ampoules containing 59 mg of a 1:3 dilution in phosphate-buffered saline (500 IU per ampoule)	1957 (3rd Standard)
Gas-gangrene antitoxin (<i>ordematiens</i>) (hyperimmune horse serum, dried)	0.082 8	Ampoules containing 91 mg (1100 IU per ampoule)	1966 (3rd Standard)
Gas-gangrene antitoxin (<i>histolyticus</i>) (hyperimmune horse serum, dried)	0.2	Bottles containing 10 ml of a solution in saline, containing 66 vol% glycerol (20 IU per ml)	1951 (2nd Standard)
Gas-gangrene antitoxin (<i>Sordelli</i>) (hyperimmune horse serum, dried)	0.133 4	Bottles containing 10 ml of a solution in saline, containing 66 vol% glycerol (20 IU per ml)	1938 (1st Standard)
Staphylococcus α antitoxin (hyperimmune horse serum, dried)	0.237 6	Bottles containing 10 ml of a solution in phosphate-buffered saline, containing 0.01 g thiomersal per 100 ml (20 IU per ml)	1938 (2nd Standard)
Scarlet fever streptococcus antitoxin (hyperimmune horse serum, dried)	0.049	Ampoules containing 490 mg (10 000 IU per ampoule)	1952 (1st Standard)
Anti-streptolysin O (human, dried)	0.021 3	Bottles containing 46 mg (2160 IU per ampoule); distributed as a 10 ml solution containing 10 IU per ml	1959 (1st Standard)
Antipneumococcus serum (type 1) (hyperimmune horse serum, dried)	0.088 6	Bottles containing 10 ml of a solution in saline, containing 66 vol% glycerol (200 IU per ml)	1934 (1st Standard)
Antipneumococcus serum (type 2) (hyperimmune horse serum, dried)	0.089 4	Bottles containing 10 ml of a solution in saline, containing 66 vol% glycerol (200 IU per ml)	1934 (1st Standard)
Anti-Q-fever serum (bovine, dried)	0.101 7	Ampoules containing 101.7 mg (1000 IU per ampoule)	1953 (1st Standard)
Antirabies serum (hyperimmune horse serum, dried)	1.0	Ampoules containing 86.6 mg (86.6 IU per ampoule)	1955 (1st Standard)
Anti-A blood-typing serum (human, dried)	0.346 5	Ampoules containing 88.7 mg (256 IU per ampoule)	1950 (1st Standard)
Anti-B blood-typing serum (human, dried)	0.352 0	Ampoules containing 90.1 mg (256 IU per ampoule)	1950 (1st Standard)
Anti-Rh ₀ (anti-D) incomplete blood-typing serum (pooled human serum, dried)	0.95	Ampoules containing 30.4 mg (32 IU per ampoule)	1966 (1st Standard)
Syphilitic human serum (dried)	3.617	Ampoules containing 177.4 mg (49 IU per ampoule)	1958 (1st Standard)
Anti-poliovirus serum (type 1) (hyperimmune monkey serum, dried)	10.78	Ampoules containing 107.8 mg (10 IU per ampoule)	1962 (1st Standard)
Anti-poliovirus serum (type 2) (hyperimmune monkey serum, dried)	10.46	Ampoules containing 104.6 mg (10 IU per ampoule)	1962 (1st Standard)
Anti-poliovirus serum (type 3) (hyperimmune monkey serum, dried)	10.48	Ampoules containing 104.8 mg (10 IU per ampoule)	1962 (1st Standard)
<i>Clostridium botulinum</i> , Type A antitoxin (hyperimmune horse serum, dried)	0.136 0	Ampoules containing 68.0 mg (500 IU per ampoule)	1963 (1st Standard)
<i>Clostridium botulinum</i> , Type B antitoxin (hyperimmune horse serum, dried)	0.174 0	Ampoules containing 87.0 mg (500 IU per ampoule)	1963 (1st Standard)
<i>Clostridium botulinum</i> , Type C antitoxin (hyperimmune horse serum, dried)	0.080 0	Ampoules containing 80.0 mg (1000 IU per ampoule)	1963 (1st Standard)
<i>Clostridium botulinum</i> , Type D antitoxin (hyperimmune horse serum, dried)	0.012 1	Ampoules containing 12.1 mg (1000 IU per ampoule)	1963 (1st Standard)
<i>Clostridium botulinum</i> , Type E antitoxin (hyperimmune horse serum, dried)	0.069 1	Ampoules containing 69.1 mg (1000 IU per ampoule)	1963 (1st Standard)
<i>Clostridium botulinum</i> , Type F antitoxin (hyperimmune rabbit serum, dried)	7.44	Ampoules containing 29.32 mg (4 IU per ampoule)	1965 (1st Standard)
<i>Naja</i> antivenin (horse serum, polyvalent [<i>Naja</i> and <i>Hemachatus</i> species], purified, dried)	2.69	Ampoules containing 807 mg (300 IU per ampoule)	1964 (1st Standard)
Anti-smallpox serum (pooled human serum, freeze-dried)	0.084 16	Ampoules containing 84.3 mg (1000 IU per ampoule)	1965 (1st Standard)
Anti-toxoplasma serum (pooled human serum, freeze-dried)	0.090 967	Ampoules containing 181.934 mg (2000 IU per ampoule)	1967 (1st Standard)

Substance	International Unit (IU) mg	Form in which dispensed	Year of establishment
aphthosa antitoxin for flocculation test (hyperimmune horse serum)	—	Bottles containing 10 ml of a dilution in phosphate-buffered saline, containing 0.01 g rhomeral per 100 ml (500 IU per ml)	1956 (4th Reference Preparation)
antiphoeb serum (hyperimmune horse serum, dried)	—	Ampoules containing dried material from 5 ml serum	1952 (1st Reference Preparation)
anti-yellow-fever serum (monkey serum, dried)	0.5	Ampoules containing 71.5 mg (143 IU per ampoule)	1962 (1st Reference Preparation)
anti-measles serum (human serum, dried)	9.378	Ampoules containing 93.8 mg (10 IU per ampoule)	1964 (1st Reference Preparation)
anti-staphylococcal P-V leucocidin serum (horse serum, freeze-dried)	0.3563	Ampoules containing 53.5 mg (150 IU per ampoule)	1965 (1st Reference Preparation)
Rheumatoid arthritis serum (pooled human serum, freeze-dried)	0.171	Ampoules containing 17.1 mg (100 IU per ampoule)	1965 (1st Reference Preparation)
Anti-rubella serum (pooled human serum, freeze-dried)	—	Ampoules containing 56.28 mg	1966 (1st Reference Preparation) (discontinued 1967)

Antibodies II

Held by International Laboratory for Biological Standards, Central Veterinary Laboratory, Weybridge, England

Anti <i>Brucella abortus</i> serum	0.09552	Ampoules containing 95.52 mg of freeze-dried bovine serum (1000 IU per ampoule)	1967 (2nd Standard)
<i>Chistidium sakaii</i> (perfringens) type D antitoxin (hyperimmune horse serum, dried)	0.0137	Ampoules containing 68.5 mg (5000 IU per ampoule)	1954 (1st Standard)
<i>Chistidium welchii</i> (perfringens) type D antitoxin (hyperimmune horse serum, dried)	0.0637	Ampoules containing 65.7 mg (1000 IU per ampoule)	1954 (1st Standard)
Swine erysipelas serum (anti-N) (hyperimmune horse serum, dried)	0.14	Ampoules containing 87.9 mg (628 IU per ampoule)	1954 (1st Standard)
Anti-swine-fever serum (pig serum, freeze dried)	0.89	Ampoules containing 889.5 mg (1000 IU per ampoule)	1963 (1st Standard)
Anti-casint-diagram serum (hyperimmune horse serum, freeze-dried)	0.0897	Ampoules containing 87.7 mg (1000 IU per ampoule)	1967 (1st Standard)
Anti-casint-hepatitis serum (hyperimmune horse serum, freeze-dried)	0.0796	Ampoules containing 79.6 mg (1000 IU per ampoule)	1967 (1st Standard)
Anti-Newcastle disease serum (chicken serum, freeze-dried)	0.1734	Ampoules containing 55.5 mg (320 IU per ampoule)	1966 (1st Reference Preparation)

Antibiotics I

Held by International Laboratory for Biological Standards, National Institute for Medical Research, London

Streptomycin (sulphate)	0.001282	Ampoules containing 175 mg (780 IU per mg)	1958 (2nd Standard)
Dihydrostreptomycin (sulphate)	0.001219	Ampoules containing 200 mg (820 IU per mg)	1966 (2nd Standard)
Bactracin (zinc bacitracin)	0.01351	Ampoules containing 100 mg (74 IU per mg)	1964 (2nd Standard)
Tetracycline (hydrochloride)	0.00101	Ampoules containing 200 mg (990 IU per mg)	1957 (1st Standard)
Chlortetracycline (hydrochloride)	0.001	Ampoules containing 60 mg (1000 IU per mg)	1953 (1st Standard)
Oxytetracycline (dihydrate)	0.0012364	Ampoules containing 100 mg (880 IU per mg)	1966 (2nd Standard)
Erythromycin (dihydrate)	0.001053	Ampoules containing 200 mg (950 IU per mg)	1957 (1st Standard)
Polymyxin B (sulphate, purified)	0.000127	Ampoules containing 19 mg (7874 IU per mg)	1955 (1st Standard)
Nystatin	0.000333	Ampoules containing 75 mg (3000 IU per mg)	1963 (1st Standard)
Amphotericin B	0.001064	Ampoules containing 100 mg (940 IU per mg)	1963 (1st Standard)
Vancomycin (sulphate)	0.000993	Ampoules containing 50 mg (1007 IU per mg)	1963 (1st Standard)
Clotrimazole (chloroform adduct)	0.001176	Ampoules containing 75 mg (850 IU per mg)	1964 (1st Standard)
Novobiose (acid)	0.001031	Ampoules containing 100 mg (978 IU per mg)	1965 (1st Standard)
Colistin (sulphate)	0.00048975	Ampoules containing 75 mg (20500 IU per mg)	1968 (1st Standard)
Rolamycin	0.001004	Ampoules containing 100 mg (996 IU per mg)	1968 (1st Standard)
Kanamycin (sulphate)	0.001232	Ampoules containing 50 mg (812 IU per mg)	1959 (1st Reference Preparation)
Kanamycin B	—	Ampoules containing 5 mg	1964 (1st Reference Preparation)
Vancomycin (sulphate)	0.00137	Ampoules containing 35 mg (730 IU per mg)	1959 (1st Reference Preparation)

Substance	International Unit (IU) mg	Form in which dispensed	Year of establishment
Antibiotics I (continued)			
Penicillin K (89.9% pure sodium <i>n</i> -heptylpenicillin, with 9.6% penicillin dihydro F and 0.5% penicillin F)	-	Ampoules containing 20 mg	1951 (1st Reference Preparation)
Neomycin (sulphate)	0.001 47	Ampoules containing 100 mg (680 IU per mg)	1958 (1st Reference Preparation)
Ristocetin	-	Ampoules containing 45 mg	1960 (1st Reference Preparation)
Ristocetin B	-	Ampoules containing 5 mg	1964 (1st Reference Preparation)
Gramicidin S	0.001 002	Ampoules containing 50 mg (998 IU per mg)	1962 (1st Reference Preparation)
Gramicidin	0.001	Ampoules containing 55 mg (1000 IU per mg)	1966 (1st Reference Preparation)
Spiramycin (base)	0.000 312 5	Ampoules containing 50 mg (3200 IU per mg)	1962 (1st Reference Preparation)
Demethylchlortetracycline	0.001	Ampoules containing 80 mg (1000 IU per mg)	1962 (1st Reference Preparation)
Triacetyloleandomycin	0.001 2	Ampoules containing 100 mg (833 IU per mg)	1962 (1st Reference Preparation)
Procaine benzylpenicillin in oil with aluminium monostearate	-	Vials containing 10 ml	1966 (2nd Reference Preparation)
Paromomycin (sulphate)	0.001 333	Ampoules containing 75 mg (750 IU per mg)	1965 (1st Reference Preparation)
Colistin methane sulphonate	0.000 078 74	Ampoules containing 75 mg (12700 IU per mg)	1966 (1st Reference Preparation)
Cephalothin (cefalotin) (sodium cephalothin)	0.001 066 1	Ampoules containing 50 mg (938 IU per mg)	1965 (1st Reference Preparation)
Lincomycin (hydrochloride)	0.001 135 1	Ampoules containing 50 mg (881 IU per mg)	1965 (1st Reference Preparation)
Capreomycin (sulphate)	0.001 087	Ampoules containing 80 mg (920 IU per mg)	1967 (1st Reference Preparation)
Rifamycin SV (sodium rifamycin SV)	0.001 127	Ampoules containing 100 mg (887 IU per mg)	1967 (1st Reference Preparation)
Gentamycin (sulphate)	0.001 56	Ampoules containing 50 mg (641 IU per mg)	1968 (1st Reference Preparation)
Lymecycline	0.001 107	Ampoules containing 50 mg (903 IU per mg)	1968 (1st Reference Preparation)
Antibiotics II			
Held by International Laboratory for Biological Standards, Central Veterinary Laboratory, Weybridge, England			
Tylosin (base)	0.001	Ampoules containing 40 mg (1000 IU per mg)	1966 (1st Standard)
Hygromycin B	0.000 892 8	Ampoules containing 40 mg (1120 IU per mg)	1966 (1st Standard)
Hormones, Vitamins, Enzymes			
Held by International Laboratory for Biological Standards, National Institute for Medical Research, London			
Oxytocin and vasopressin (antidiuretic hormone) for bioassay (posterior ox pituitary, acetone-dried, powdered)	0.5	Ampoules containing 30 mg (2 oxytocic, 2 vasopressor and 2 antidiuretic IU per mg)	1957 (3rd Standard)
Prolactin for bioassay (active principle from anterior sheep pituitary, dried)	0.045 45	Ampoules containing 10 mg (22 IU per mg)	1962 (2nd Standard)
Corticotropin (ACTH) for bioassay (from anterior pig pituitary, purified)	1.0	Ampoules containing 50 mg with lactose, freeze-dried (1 IU per mg)	1962 (3rd Standard)
Thyrotropin for bioassay (from anterior ox pituitary, purified)	13.5	Ampoules containing ten 20-mg tablets of a blend of 1 part thyrotropin and 19 parts lactose (ca. 1.48 IU per tablet)	1954 (1st Standard)
Growth hormone for bioassay (active principle from anterior ox pituitary, dried)	1.0	Ampoules containing 30 mg (1 IU per mg)	1955 (1st Standard)
Growth hormone for immunoassay (from human anterior pituitary, purified)	24.29	Ampoules containing 8.5 mg with sucrose (0.350 IU per ampoule)	1968 (1st Reference Preparation)

Substance	International Unit (IU) mg	Form in which dispensed	Year of establishment
Human menopausal gonadotropins for bioassay (active principle from urine of post-menopausal women, freeze-dried)	0 229 5	Ampoules containing 9 mg diluted with lactose (40 follicle-stimulating hormone IU and 40 interstitial cell-stimulating hormone IU per ampoule)	1964 (2nd Reference Preparation)
Serum gonadotropin for bioassay (from serum of pregnant mares)	0 003 569	Ampoules containing 5.71 mg with lactose, freeze-dried (1600 IU per ampoule)	1966 (2nd Standard)
Chorionic gonadotropin for bioassay (active principle from human urine of pregnancy)	0 001 279	Ampoules containing 7 mg diluted with lactose, dried (5300 IU per ampoule)	1963 (2nd Standard)
Insulin for bioassay (52% bovine and 48% porcine pancreas, purified)	0 041 67	Ampoules containing 110-125 mg (24 IU per mg)	1958 (4th Standard)
Erythropoietin for bioassay (from human urine)	1 48	Ampoules containing 14.80 mg with lactose (0.675 7 IU per mg)	1965 (1st Reference Preparation)
Heparin (sodium salt of purified active principle from bovine lung tissue)	0 007 7	Ampoules containing 20 mg (130 IU per mg)	1958 (2nd Standard)
Vitamin D ₂	0 000 025	Bottles containing 6 g of a solution in vegetable oil (1000 IU per g)	1949 (2nd Standard)
Vitamin B ₁₂ (cyanocobalamin)	-	Ampoules containing ten 20-mg tablets	1959 (1st Reference Preparation)
Hyaluronidase (from bovine testes, dried)	0 1	Ampoules containing ten 20-mg tablets diluted with lactose (ca 200 IU per tablet)	1955 (1st Standard)
Streptokinase-streptodornase (active material, dried)	-	Ampoules containing 1 mg with 5.5 mg of lactose (3100 streptokinase IU and 2400 streptodornase IU per ampoule)	1964 (1st Standard)
Streptokinase	0 002 890		
Streptodornase	0 002 700		
Urokinase (from human urine, purified)	0 001 410	Ampoules containing 6.77 mg with lactose, freeze-dried (480 IU per ampoule)	1968 (1st Reference Preparation)

Miscellaneous I

Held by International Laboratory for Biological Standards, National Institute for Medical Research, London

Digitalis (dry powdered leaf of <i>Digitalis purpurea</i>)	75 0	Ampoules containing 2500 mg (0.013 16 IU per mg)	1949 (3rd Standard)
Neomphenamine	-	Ampoules containing 300 mg	1940 (3rd Reference Preparation)
Sulphamphenamine	-	Ampoules containing 300 mg	1951 (3rd Reference Preparation)
Oxyphenamine (hydrochloride)	-	Sets of 3 ampoules containing (a) 120 mg oxyphenamine hydrochloride (b) 100 mg anhydrous sodium carbonate (c) 500 mg anhydrous sucrose	1951 (1st Reference Preparation)
Mel B (melamyl-4-phenylarsenochingipicrate)	-	Ampoules containing 100 mg	1954 (1st Reference Preparation)
MSb (sodium β -melamylphenylisobutylphosphate polymer)	-	Ampoules containing 500 mg	1954 (1st Reference Preparation)
Dimercaprol (B.L. 2,3-dimercaptopropanol)	-	Ampoules containing 2 ml	1952 (1st Reference Preparation)
Protamine	-	Ampoules containing 60 mg	1954 (1st Reference Preparation)
Pyrogen (purified 'O' antigen of <i>Shigella dysenteriae</i> dried)	-	Ampoules containing 2 mg	1958 (1st Reference Preparation)

Miscellaneous II

Held by International Laboratory for Biological Standards, Statens Serum Institut, Copenhagen

Opacity reference preparation (aqueous suspension of pyrex glass particles)	-	Ampoules containing 15 ml (10 IU of opacity per ml)	1953 (3rd Reference Preparation)
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Miscellaneous III

Held by Rijks Instituut voor de Volksgezondheid, Utrecht

Haemoglobinacide reference preparation	-	Ampoules containing 10 ml of haemoglobinacide 15.5 units	1947 (1st Reference Preparation)
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Substance	Form in which dispensed	Year of establishment
International Biological Reference Reagents Reference Reagents I Held by International Laboratory for Biological Standards, Statens Seruminstitut, Copenhagen		
Anti-tick-borne encephalitis sera: Anti-tick-borne encephalitis serum (louping ill (Moredu) virus) Anti-tick-borne encephalitis serum (Russian spring-summer encephalitis (SOPHYN and ANSETTAROV) virus) Cholera agglutinating serum (OGAWA) Anti-trichinella human serum Enterovirus antisera: Coxsackie virus antisera types A9, B1, B2 and B3 Coxsackie virus antisera types B4 and B5 Echovirus antisera types 1, 2, 3, 4, 5, 6, 6 ¹¹ , 7, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 and 25 Poliovirus antisera types 1, 2 and 3 Reovirus antiserum type 1 Adenovirus antisera: Types 1, 2, 3, 5, 6, 7a, 8, 9, 10, 11, 13, 15 and 17 Types 12 and 18 Parainfluenza virus antisera: Types 1, 2 and 3 Mycoplasma pneumoniae antiserum	Ampoules containing 1 ml of freeze-dried sheep serum Ampoules containing 2 ml of freeze-dried sheep serum Ampoules containing 1 ml of monospecific serum Ampoules containing 1 ml of freeze-dried pooled human serum Ampoules containing 0.5 ml of freeze-dried monkey serum Ampoules containing 0.5 ml of freeze-dried monkey serum Ampoules containing 0.5 ml of freeze-dried horse serum Ampoules containing 0.5 ml of freeze-dried horse serum Ampoules containing 0.5 ml of freeze-dried horse serum	1964 (1st Reference Reagent) 1967 (1st Reference Reagent) 1968 (1st Reference Reagent) 1965 (1st Reference Reagent) 1966 (1st Reference Reagent) 1966 (1st Reference Reagent) 1967 (1st Reference Reagent) 1968 (1st Reference Reagent)
Reference Reagents II Held by WHO/FAO and WHO Leptospirosis Reference Laboratories		
Anti- <i>Leptospira</i> sera: Anti- <i>Leptospira interrogans</i> serotype <i>saxkoebing</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>castellonis</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>sejroe</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>mini</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>australis</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>copenhagensis</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>tarassovi</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>autumnalis</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>rachmatii</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>pomona</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>bataviae</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>hebdomadis</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>andamana</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>javanica</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>pyrogenes</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>naam</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>mankarto</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>sarmin</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>poi</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>schueffneri</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>muenchen</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>synopteri</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>bangkinang</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>wolffi</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>hardjo</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>kremslos</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>benjamin</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>zanoni</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>medanensis</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>paidjan</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>semaranga</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>canicola</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>grippityphosa</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>icterohaemorrhagiae</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>atlantae</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>georgia</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>bratislava</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>erinacei-aurati</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>taxi</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>fugis</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>worfoldi</i> serum Anti- <i>Leptospira interrogans</i> serotype <i>malaya</i> serum	Ampoules containing 0.5 ml or 1.0 ml of hyperimmune rabbit serum, dried Ampoules containing 0.5 ml or 1.0 ml of hyperimmune rabbit serum, dried Ampoules containing 1.0 ml of hyper-immune rabbit serum, dried Ampoules containing 0.5 ml of hyper-immune rabbit serum, dried Ampoules containing 0.5 ml or 1.0 ml of hyperimmune rabbit serum, dried	1958 (1st Reference Reagent) 1962 (1st Reference Reagent) 1962 (2nd Reference Reagent) 1966 (2nd Reference Reagent) 1966 (1st Reference Reagent)

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- Adenosine triphosphate (*contd.*), in blood . . . 577
- in carbohydrate synthesis and breakdown . . . 441
 - in carbon-chain extension . . . 424
 - catecholamine complexes . . . 731
 - in cephalin formation . . . 425
 - in cholesterol formation . . . 426
 - in coenzyme A formation . . . 345, 487
 - reaction with creatine . . . 437, 438
 - in degradation of fats . . . 391, 392
 - in fatty acid synthesis from citrate . . . 424, 425
 - in glutathione formation . . . 438
 - in formation of glycine conjugates . . . 444, 445
 - in glycolysis . . . 389
 - in guanidyl acid formation . . . 436
 - in inosinic acid formation . . . 433, 435
 - in isoleucine degradation . . . 396
 - in lactic acid fermentation . . . 390
 - in lecithin formation . . . 425
 - in leucine degradation . . . 395, 396
 - in L-methionine degradation . . . 398
 - in NAD and NADP formation . . . 477
 - in transfer of one-carbon groups . . . 437
 - in pantothenic acid formation . . . 487
 - in detoxication of phenylacetic acid . . . 445
 - in phosphatidic acid formation . . . 375
 - in pyrimidine formation . . . 439
 - in spermatozoa . . . 684
 - in sulphate ester formation . . . 445
 - in thiamine formation . . . 470
 - in urea formation . . . 442 sq.
 - in vitamin B₁₂ formation . . . 484
- S-Adenosylhomocysteine, in creatine formation . . . 437
- in L-methionine degradation . . . 398
- S-Adenosylmethionine, in creatine formation . . . 437
- in L-methionine degradation . . . 398
- Adenovirus antisera, reference reagents . . . 764
- Adenylate cyclase, effect of catecholamines . . . 733
- Adenylate kinase, in synthesis of ATP . . . 404
- in plasma . . . 595
- 5'-Adenylic acid. See Adenosine monophosphate
- Adenylosuccinate lyase in adenylic acid formation . . . 436
- Adenylosuccinic acid . . . 342
- in adenylic acid formation . . . 435, 436
- Adermine. See Pyridoxine
- ADH. See Alcohol dehydrogenase
- ADH (antidiuretic hormone). See Vasopressin
- Adipic acid in urine . . . 674
- Adipohepatic liver, serum enzyme changes . . . 586
- Adipose tissue. See under Tissues
- Ado. See Adenosine
- Adolescence, basal metabolism . . . 539
- blood, acid phosphatase . . . 596
 - alkaline phosphatase . . . 596
 - aspartate aminotransferase . . . 593
 - calcium . . . 565
 - fructosediphosphate aldolase . . . 599
 - glucose . . . 605
 - growth hormone . . . 720
 - iodine . . . 564
 - lactate dehydrogenase . . . 590
 - magnesium . . . 566
 - inorganic phosphorus . . . 563
 - potassium . . . 564
 - proteins . . . 583
 - thyroid hormone . . . 726
 - thyroxine breakdown . . . 727
 - blood pressure . . . 553
 - blood volume . . . 554, 555
 - body weight . . . 711
 - bone marrow cells . . . 621
 - erythrocytes, count . . . 614, 617
 - diameter . . . 617
 - sedimentation rate . . . 558
 - mean corpuscular volume . . . 617
 - haematocrit . . . 617
 - haemoglobin . . . 617
 - iodide metabolism . . . 726
 - leucocyte count . . . 618, 619
 - lung values . . . 550
 - organ weights . . . 710
 - reticulocyte count . . . 613
 - development of teeth . . . 709
 - urine, corticosteroids . . . 747 sq.
 - gonadotropins . . . 714
 - pregnanediol . . . 754
 - testosterone . . . 752
 - volume . . . 661
 - vitamin B₆ requirement . . . 475
- Adonitol . . . 322
- D-Adonose. See D-Ribulose
- ADP. See Adenosine diphosphate
- Adrenals, ascorbic acid . . . 490
- catecholamines . . . 731
 - cholesterol synthesis . . . 426
 - corticosteroids . . . 743, 746
 - hyperplasia . . . 456
 - lactic acid fermentation . . . 388
 - phenylethanolamine N-methyltransferase . . . 440
 - phospholipase A . . . 417
 - respiratory rate . . . 387
 - weight . . . 710
- Adrenal cortex, effect of ACTH . . . 430, 717
- androgens . . . 751
 - in cardiac infarction . . . 624
 - functional tests . . . 747
 - hormones. See Corticosteroids
 - insufficiency, sodium in sweat . . . 680
 - urinary secretion . . . 661
 - oestrogens . . . 755
 - pituitary control . . . 430
 - progesterone secretion . . . 753
- Adrenaline . . . 730
- in cyclic AMP formation . . . 345
 - biosynthesis . . . 440, 731
 - in blood . . . 731, 733
 - breakdown . . . 732
 - and haemorrhagic diatheses . . . 623, 624
 - release . . . 731
 - in urine . . . 668, 733
- Adrenal medulla, in cardiac infarction . . . 623, 624
- catecholamine formation . . . 731
- Adrenochrome from adrenaline . . . 731
- Adrenocortical hormones. See Corticosteroids
- Adrenocorticotrophic hormones. See Corticosteroids
- Adrenocorticotrophic hormone. See Corticotropin
- Adrenocorticotropin. See Corticotropin
- Adrenogenital syndrome and ossification . . . 707
- Adrenoglomerulotropin . . . 730
- Adrenosterone . . . 379
- biosynthesis . . . 428, 429
- Actianedione . . . 379
- Actiocholandione . . . 379
- Actiocholanolone . . . 379
- in urine . . . 746, 749
- 3 β -Actiocholanolone . . . 379
- Actiocobalamin . . . 483
- Actioporphyrins . . . 355
- Ag. See Silver
- Agglutinins in erythrocyte sedimentation . . . 559
- Agglutinins, cold, in erythrocyte sedimentation . . . 559
- Ag groups of serum . . . 634
- Aglycons . . . 308
- Air (*see also Atmosphere*), molecular weight . . . 252
- radiation absorbed by . . . 220
 - standard, in spectroscopy . . . 230
 - sea level standard values . . . 252
 - standard density . . . 230
- Al. See Aluminium
- Ala. See α -Alanine
- Alactasia . . . 451
- α -Alanine (*L*-alanine) (Ala) . . . 330
- in blood . . . 574
 - in blood proteins . . . 581
 - degradation . . . 394, 402
 - in foods . . . 516
 - formation from glucose . . . 420
 - in milk . . . 688
 - in saliva . . . 645
 - in sweat . . . 680
 - in transamination reactions . . . 394
 - in tryptophan degradation . . . 399
 - in urine . . . 667
- β -Alanine . . . 334
- in blood . . . 574
 - in degradation of cytosine and uracil . . . 401
 - formation from aspartic acid . . . 394, 434
 - function . . . 434
 - oxidation . . . 401
 - in pantothenic acid synthesis . . . 487
 - in saliva . . . 645
 - in transamination reactions . . . 394
 - in urine . . . 667
- Alanine aminotransferase, activity, gradients . . . 586
- temperature correction . . . 585
 - in blood . . . 585, 594
 - half-life . . . 586
 - in heart disease . . . 587
 - in liver disease . . . 586, 587
 - effect of muscular work . . . 586
 - in pregnancy . . . 586
 - in cerebrospinal fluid . . . 638
- Alanine aminotransferase, in gastric juice . . . 650
- in milk . . . 689
 - in saliva . . . 645
 - in seminal plasma . . . 684
 - in synovial fluid . . . 641
 - in tissues . . . 585
- L-Alanine: 2-oxoglutarate aminotransferase. See Alanine aminotransferase
- Alanyl-transfer RNA . . . 351
- Albinism . . . 448
- Albumins . . . 329
- Albumin (serum albumin), amino-acid composition . . . 581
- in bile . . . 655
 - in blood . . . 580, 582, 583
 - in cerebrospinal fluid . . . 637
 - characteristics and function . . . 580
 - in faeces . . . 659
 - in gastric juice . . . 650
 - glomerular filtration and excretion . . . 536
 - in intestinal juice . . . 656
 - lipid complex, in erythrocyte sedimentation . . . 559
 - metabolism . . . 579
 - in milk . . . 688, 689
 - osmotic activity . . . 526
 - in pancreatic juice . . . 652
 - activation of phospholipase A . . . 417
 - in saliva . . . 645
 - in semen . . . 684
 - in synovial fluid . . . 641
 - tagged, enteral excretion test . . . 289
 - in urine . . . 668
- Alcohol. See Ethanol
- Alcohols, complex cyclic, as lipid components . . . 365
- conjugation . . . 442
 - higher aliphatic, in faeces . . . 659
 - in lipids . . . 365
 - polyhydric . . . 312, 322
- Alcohol dehydrogenase, in plasma . . . 590
- in isomerization of retinal . . . 460
 - in tissues . . . 585
 - in vitamin A metabolism . . . 457
- Alcoholic beverages, composition . . . 509
- Alcoholic fermentation . . . 387, 390
- Alcohol: NAD oxidoreductase. See Alcohol dehydrogenase
- ALD (aldolase). See Fructosediphosphate aldolase
- Aldehyde-lyases . . . 366
- Aldehyde oxidase, in vitamin A metabolism . . . 457
- in vitamin B₆ interconversions . . . 473
- Aldolase. See Fructosediphosphate aldolase
- Aldonic acids . . . 312, 323
- Aldoses . . . 308 sq.
- Aldosterone . . . 379, 430, 743 sq.
- in adrenals . . . 743
 - biological activity . . . 749
 - biosynthesis . . . 428, 429
 - in blood . . . 745
 - breakdown . . . 746, 747
 - secretion, effect of ACTH . . . 717
 - effect of angiotensin . . . 741
 - inborn limitation . . . 456
 - effect of progesterone . . . 754
 - rates . . . 743, 745
 - in urine . . . 746, 747
- Aldo-sugars . . . 308 sq.
- Alisterase . . . 414
- Aliphatic acids, conjugation . . . 442
- Alizarin yellow indicators . . . 283
- Alkaline phosphatase. See Phosphatase, alkaline
- Alkalosis . . . 569
- metabolic . . . 528
 - respiratory . . . 527
 - urinary acidity in . . . 448
- Alkaptonuria . . . 675
- homogenetic acid excretion in . . . 374
- Alkoxydiglycerides . . . 365, 374
- Alkylglucuronides, formation in detoxication . . . 442
- Alkyl lysophosphatide ethers . . . 365
- Alkylxylylphosphatides . . . 401
- Allantoic acid in purine degradation . . . 577
- Allantoin, in plasma . . . 400, 401
- in purine degradation . . . 419
 - from uric acid . . . 671
 - in urine . . . 755
- ALLN-Doisy test . . . 351
- Allo-compounds . . . 379
- Allocholol . . . 379
- β -Allocholol . . . 379
- Allochololone . . . 379
- β -Allochololone . . . 379
- α -Allopregnanediol . . . 377

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- Anaemia (*contd.*), erythrocyte coproporphyrin 575
 - erythrocyte osmotic resistance 616
 - erythrocyte protoporphyrin 576
 - haemolytic 454
 - - pyruvate kinase in 594
 - - serum bilirubin in 577
 - macrocytic, in folic acid deficiency 479
 - - in vitamin B₁₂ deficiency 485
 - megaloblastic 453
 - - in folic acid deficiency 479, 610
 - - serum glucosephosphate isomerase in 600
 - - in vitamin B₁₂ deficiency 610
 - microcytic 448
 - pernicious, diagnosis from gastric juice 650
 - - gastric acidity and 648
 - - gastric juice carbohydrates in 650
 - - pyridoxine-deficiency 476
 - - pyridoxine-sensitive 476
 - in scurvy, ascorbic acid and 490
 - sickle-cell 446, 447
 - - blood viscosity in 558
 ANDERSEN'S disease 450, 451
 Androgens 379 sq., 751 sq.
 - biological activity 752, 753, 758
 - biosynthesis 428, 429
 - inborn excess 456
 - in blood 751, 752
 - in semen 685
 Androstane 381
 5 α -Androstane-3,17-dione 379, 751 sq.
 5 β -Androstane-3,17-dione 379
 Androstan-3 α -ol-17-one. See Androsterone
 Δ^4 -Androstene-3,17-dione 379, 751 sq.
 - biosynthesis 428, 429
 - breakdown 746
 - in oestrogen synthesis 431
 - in testes 746
 Androst-4-ene-3,11,17-trione. See Adrenosterone
 Androstenedione. See Dehydroepiandrosterone
 Androsterone 379, 751 sq.
 - in urine 430, 746, 749
 Anemia. See Anaemia
 Anosinophilia 620
 Aneurin. See Thiamine
 Angina pectoris, serum enzyme changes 587
 Angioneurotic oedema, plasma kinins 742
 Angiotensin 740, 741
 Angiotensinase 740
 Angiotonin 740, 741
 Angles 138, 139
 - units 138, 207, 208
 Ångström 200, 202
 Angular acceleration units 211
 - frequency units 208
 - momentum, quantum-mechanical unit 228
 - velocity units 210
 Anhydro-compounds 381
 Animal protein factor 482
 Anocstrin 730
 Anomalistic year 206
 ANSBACHER unit for vitamin K 467
 Asnerine in urine 666
 Anteismargaric acid 371
 Anterior pituitary. See under Pituitary
 Anthranilic acid, in tryptophan degradation 398, 399, 475
 - in urine 669
 Antibiotics, standards and reference preparations 761, 762
 Antibodies, blood-group specific, clinical importance 632, 633
 - action of corticosteroids 750
 - formation, pyridoxal phosphate in 475
 - carried by immunoglobulins 580
 - standards and reference preparations 760, 761
 Anticoagulants, use in thrombo-embolism 622
 Anticodons 353
 Antidiuretic hormone. See Vasopressin
 Antidiuretin. See Vasopressin
 Antigens, infrequent 632
 - private 632
 - public 632
 - standards and reference preparations 759
 - widely distributed 632
 Antigen-antibody reaction 626
 Anti-inflammatory steroids 379, 380
 Antilogarithms, common four-place 134, 135
 - explanation 56
 Antilogits and logits 56
 Antilysozymes 622
 Antimony, properties, isotopes, etc. 239
 Antimony-124, characteristics 293
 Antiplasmin 622
 Antirachitic activity 462 sq.
 Antiscra, standards and reference preparations 760, 761
 Antistreptolysin O, standard 760
 Antitoxins, standards and reference preparations 760
 α_1 -Antitrypsin, amino-acid composition 581
 - characteristics and function 580
 - in serum 580
 Anuria 661
 Aorta, nomogram for diameter and biological age (inside back cover)
 ap (apothecaries' measure) 205
 Apocrine sweat. See Sweat
 Apo-enzymes 382
 Apostilb 223
 apoth (apothecaries' measure) 205
 Apothecaries' units 204, 205
 Apotransaminases in vitamin B₆ interconversions 473
 Apples, composition 499
 Apple juice, composition 499
 - sauce, composition 499
 Apricots, composition 499
 Aquocobalamin 482, 483
 Ar (argon) 235
 D-Arabinose 310, 313
 - in bile 655
 - in saliva 646
 - in urine 673
 L-Arabitol 322
 D-Arabinulose. See D-Ribulose
 Arachidic acid 367
 - in brain gangliosides 377
 - in milk 687
 Arachidonic acid 370, 492
 - in blood lipids 604
 - dietary requirements 495
 - in foods 498 sq.
 - in lecithins 375
 - in milk 687
 Arc functions 139
 Arc measure 138
 Arc sine 139
 - tables 69
 Arc 203
 Area units 202, 203
 Arg. See L-Arginine
 Arginase in plasma 598
 - in urea cycle 442, 443
 L-Arginine (Arg) 330
 - in blood 574
 - in blood proteins 581
 - cell constituents from 434
 - creatine from glycine, methionine and 437
 - degradation 394, 395, 402
 - in foods 516
 - in milk 688
 - in saliva 645
 - in semen 683
 - in sweat 680
 - in transamination reactions 394
 - in urea synthesis 443, 444
 - in urine 452, 667
 L-Arginine amidinohydrolase. See Arginase
 Arginine vasopressin 724
 Arginine vasotocin 724
 Argininosuccinate, in urea synthesis 442 sq.
 - in urine 449
 Argininosuccinate lyase, in argininosuccinic aciduria 449
 - in urea cycle 442, 443
 Argininosuccinate synthetase, in citrullinaemia 449
 - in urea cycle 442, 443
 Argininosuccinic acid (see also Argininosuccinate) 334
 Argon, properties, isotopes, etc. 235
 Arg⁺-vasopressin 724
 Ariboflavinosis 473
 Arie acids (saccharic acids) 137
 - series 136, 137
 Arms, surface area 528
 - circumference during growth 695 sq.
 Aromatic acids. See under Acids
 Arsenic, atomic weight multiples 250
 - in blood 567
 - properties, isotopes, etc. 236
 - in urine 664
 Arsenic-74, characteristics 292
 - diagnostic use 289
 Arsenic-76, characteristics 292
 Arterial blood, carbon dioxide pressure 545
 Arterial blood, oxygen pressure and saturation 544
 - pH value 545, 560
 - viscosity 558
 - volume 554
 Arterial blood pressure 553
 Arthritis. See Rheumatoid arthritis
 Arterioles, composition 502
 Arylesterase in milk 689
 Arylglucuronide formation in detoxication 442
 Arylsulphatases in urine 672
 As. See Arsenic
 asb (apostilb) 223
 ASCHHEIM-ZONDEK test 715
 Ascorbic acid (L-ascorbic acid) 323, 489, 490
 - in blood 490, 611
 - in body fluids and tissues 489, 490
 - in cerebrospinal fluid 639
 - deficiency 490
 - dietary requirements 490, 494
 - in faeces 660
 - in foods 499 sq.
 - losses during cooking 498
 - in gastric juice 650
 - in milk 659
 - redox system 490
 - in saliva 646
 - in semen 685
 - in synovial fluid 642
 - in urine 676
 Asn. See Asparagine
 Asp. See L-Aspartic acid
 Asparagine (Asn, Asp[NH₂]) 330
 - in blood 574
 - in urine 667
 Asparagus, composition 502
 Aspartate aminotransferase, activity, gradients 585
 - temperature correction 585
 - in blood 585, 593
 - half-life 585
 - in heart disease 587
 - in liver disease 586, 587
 - in muscle disease 587
 - effect of muscular work 586
 - in pregnancy 585
 - cell binding 585
 - in cerebrospinal fluid 638
 - in gastric juice 650
 - isozymes 584
 - in milk 689
 - in saliva 645
 - in seminal plasma 684
 - in synovial fluid 641
 - in tissues 585
 - in urine 672
 Aspartate carbamoyltransferase in pyrimidine synthesis 439
 L-Aspartate: 2-oxoglutarate aminotransferase. See Aspartate aminotransferase
 L-Aspartic acid (Asp) 330
 - in adenylic acid formation 435
 - in blood 574
 - in blood proteins 581
 - cell constituents from 434
 - decarboxylation 394
 - degradation 394, 402
 - in foods 516
 - formation from glucose 420
 - in inosinic acid formation 688
 - in milk 438, 439
 - in pyrimidine synthesis 645
 - in saliva 680
 - in sweat 394
 - in transamination reactions 442 sq.
 - in urea synthesis 442 sq.
 - in urine 667
 Aspartic acid β -monoamide. See Asparagine
 Asp(NH₂). See Asparagine
 Associative law 244
 Astatine, properties, isotopes, etc. 290, 291
 Astronomical unit 206
 - year 212
 at (technical atmosphere) 242
 At (astatine) 456
 Atheroma 212
 atm (physical atmosphere) 234 sq.
 Atmosphere (see also Air), composition 252 sq.
 - ICAO Standard 212
 Atmosphere (pressure unit) 274
 Atom, definition 229
 Atomic constants 228, 229
 - mass constant 226, 227
 - mass scale 213, 226, 227
 - mass unit 213, 226, 227

ATP AMP phosphotransferase See Adenylate kinase
ATPase in milk 689
ATP creatine phosphotransferase See Creatine kinase
ATP D-fructose 1-phosphotransferase See Kethohexokinase
ATP D-hexose 6-phosphotransferase See Hexokinase
ATP 3-phospho-D-glycerate 1-phosphotransferase See Phosphoglycerate kinase
ATP pyruvate phosphotransferase See Pyruvate kinase
ATPS (ambient temperature and pressure, saturated) 54
atto- (10^{-18}) 5
Aw See Gold

[illegible]

- Blood (*contd.*), haemoglobin 576
 - haemoglobin 576, 579, 615, 617
 - histamine 575
 - β -hydroxybutyric acid 608
 - hydroxyproline 449
 - inosine triphosphate 577
 - iron 566
 - isoleucine 449
 - α -ketoglutaric acid 607
 - α -ketoisovaleric acid 608
 - α -ketoisovaleric acid 607
 - α -keto- β -methylvaleric acid 608
 - ketone bodies 608
 - lactic acid 607
 - lead 567
 - leucine 449
 - lipids 600 sq.
 - - excess 374, 456
 - malic acid 607
 - manganese 567
 - mercury 567
 - methylguanidine 573
 - 5-methyltetrahydropteroylglutamic acid 610
 - molybdenum 567
 - nicotinamide-adenine dinucleotide 577
 - nicotinamide-adenine dinucleotide phosphate 577
 - nicotinic acid 477, 610
 - nitrite 564
 - total nitrogen 572
 - nitrogenous substances 572 sq.
 - non-nitrogenous metabolites 606 sq.
 - nonprotein nitrogen 572
 - nucleotides 577
 - osmolality 557
 - osmotic pressure 557
 - oxalic acid 607
 - oxaloacetic acid 608
 - oxygen values 570
 - pantothenic acid 488, 611
 - pH value 560
 - phenylalanine 448
 - phosphoric esters 563
 - phosphorus 563
 - physicochemical data 557 sq.
 - porphyrins 575 sq.
 - proline 449, 574
 - propionic acid 607
 - proteins 579
 - protein sulphur 563
 - prothrombin deficiency 449, 467, 468
 - unconjugated pterins 610
 - purines 577
 - pyridoxie acid 610
 - pyruvic acid 607
 - redox potential 560
 - reducing substances 604, 605
 - riboflavin 471, 609
 - rubidium 567
 - selenium 567
 - serotonin 575
 - silicate 564
 - specific gravity 557
 - specific heat 560
 - spermidine 575
 - spermine 575
 - sulphur 563
 - thiamine 470, 609
 - tin 567
 - tryptamine 575
 - tyrosine 449
 - urea 572
 - uric acid 577
 - uridine diphosphate 577
 - valine 449
 - verdoglobulin 576
 - viscosity 558
 - - and haematocrit 557
 - vitamins 609 sq.
 - vitamin B₆ 475, 609
 - vitamin B₁₂ 610
 - volume 528, 554 sq.
 - - nomogram 556
 - - gain in pregnancy 691
 - - pulmonary and intrapulmonary 544
 - - tracer study 289
 - water 561
 - zinc 567
 Blood circulation. See Circulation
 Blood-clot retraction 622, 625
 - time 625
 Blood coagulation. See under Blood
 Blood diseases, radiotherapy 291
 - serum enzyme changes 587
 Blood groups 626 sq.
 - clinical significance 632, 633
 - mother-and-child incompatibility 611
 Blood-group substances, action of β -acetylglucosaminase 413
 - biosynthesis 424
 - in faeces 659
 - in gastric juice 650
 - in saliva 645
 - secretion 627
 - secretor character for 631
 Blood platelets. See Thrombocytes
 Blood pressure 553, 554
 - effect of angiotensin 741
 - capillary 526, 554
 - effect of oxytocin and vasopressin 723, 724
 - pulmonary 544
 Blood sugar. See D-Glucose
 Blood-typing sera, standards 760
 Blood vessels, pressure relationships 544
 Blood volume. See under Blood
 BMR. See Basal metabolism
 BODANSKY enzyme units 584
 Body, composition 517 sq.
 - - approximate 523
 - - elementary 234 sq.
 - - fluids, electrolyte composition 523, 525
 - - enzyme activities 585
 - - extracellular. See Extracellular fluid
 - - interstitial. See Interstitial fluid
 - - intracellular. See Intracellular fluid
 - - intraluminal, amount and electrolytes 525
 - - intravascular, amount and electrolytes 525
 - haematocrit. See Haematocrit
 - height changes during growth 695 sq.
 - length, of embryo 691
 - - of foetus 691, 692
 - - of infants 693 sq.
 - measurements during growth 693 sq.
 - metabolic size 473
 - organs, weights 710
 - parts, surface areas 528
 - surface area, age and 528
 - - dietary requirements from 524
 - - of adults, nomogram 537
 - temperature and pressure, saturated (BTPS) 260, 541
 - type, blood volume and 528
 - - caloric requirement and 495
 - water (*see also* Water), balance. See Water balance
 - - extracellular. See Extracellular fluid
 - - glomerular filtration and excretion 536
 - - insensible loss 524
 - - intracellular. See Intracellular fluid
 - - gain in pregnancy 690
 - - total 517, 518, 523
 - weight, of adolescents 711
 - - of adults, average 711
 - - desirable 712
 - - and blood volume 555
 - - and caloric requirement 495
 - - of children 695 sq.
 - - gastric acidity and 648
 - - of embryo 691
 - - of foetus 691, 692
 - - of infants 693 sq.
 - - of newborn 692, 693
 - - loss during first days 692
 - - during pregnancy 690
 - - proportions of brain, fat and muscle 517
 Bohr magneton 229
 Bohr radius 228
 Boiling point of elements 234 sq.
 BOLTZMANN entropy constant 228
 Bombay phenotypes 627
 Bone, alkaline phosphatase 415
 - barium 521
 - composition 521
 - cortical, composition 521
 - development 706 sq.
 - disease, serum alkaline phosphatase in 596
 - organic components 522
 - parathyroid hormone and 728
 - radiation absorbed by 220
 - strontium 521
 - strontium-90:calcium ratio 521
 - tumours, leucocyte mobility 560
 - role of vitamin D 461
 Bone marrow 621
 - lactic acid fermentation 388
 - lipid accumulation 455
 - respiratory rate 387
 Borate, in blood 564
 Borate, in whole body 517
 - in lungs 519
 - in urine 664
 Borax, solutions, decinormal 277
 - pH values 279
 Boric acid, solutions, decinormal 277
 - pH values 279
 Boron, flame lines 284
 - properties, isotopes, etc. 234
 Br. See Bromide and Bromine
 Bradykinin 742
 BRAGG-GRAY conditions 219, 220
 Brain, β -acetylglucosaminase 413
 - animal, amino acids 516
 - - composition 512, 513
 - ascorbic acid 489
 - biotin 486
 - contribution to BMR 539
 - catecholamines 731
 - cholinesterase 414
 - composition 519, 520
 - degeneration 455, 456
 - gangliosides. See under Gangliosides
 - lactic acid fermentation 388
 - lipids 369, 372, 377
 - phosphatases 416
 - phospholipase C 417
 - purine nucleoside phosphorylase 418
 - radiography 289
 - respiratory rate 387
 - thiamine 470
 - transaminations 394
 - vitamin B₆ 475
 - weight 710
 - - proportional 517
 Brain sugar. See D-Galactose
 Brandy, composition 509
 Brassidic acid 369
 Brazil nuts, amino acids 516
 - composition 507
 Bread, amino acids 516
 - composition 507, 508
 Breasts. See Mammary glands
 Breast feeding, effect on urinary amino acids 667
 - effect on urinary electrolytes 663, 664
 - effect on urinary nitrogen 665, 666
 - effect on infants' stools 657
 - effect on serum tocopherols 609
 Breast milk. See under Milk
 Breathing capacity, maximum (MBC) 543
 BREDDIN's method 625
 Bremsstrahlung 218
 - absorbed dose from 220
 British thermal unit 213
 BRITTON-ROBINSON buffer 280 sq.
 Broad beans, composition 503
 Broccoli, amino acids 516
 - composition 503
 Bromhidrosis 679
 Bromide, in blood 563
 - in cerebrospinal fluid 649
 - in gastric juice 644
 - in saliva 644
 - decinormal solutions 277
 - in sweat 679
 - in urine 663
 - in urine 250
 Bromine, atomic weight multiples 237
 - properties, isotopes, etc. 292
 Bromine-82, characteristics 292
 - decay table 299, 300
 Bromochlorophenol blue indicator 283
 Bromocresol green indicator 283
 Bromocresol purple indicator 283
 Bromophenol blue indicator 283
 Bromothymol blue indicator 283
Brucella abortus antiserum, standard 761
 BRUNN enzyme units 516
 Brussels sprouts, amino acids 503
 - composition 627
 B substance, secretion 627
 BTPS (body temperature and pressure, saturated) 260, 541
 Bru (British thermal unit) 213
 bu (bushel) 203, 204
 BÜCHER enzyme units 508
 Buckwheat flour, composition 280 sq.
 Buffer solutions 573
 Bufotenine, in blood 649
 - in urine 204
 Bushel 204
 Butanoic acid. See α -Butyric acid
 Butenoic acids 368
 Butter, composition 510
 Buttermilk, composition 511

A detailed index to the statistical tables (pages 28-131) and chapters on Statistical Methods (pages 146-196) will be found on pages 197-198.

[illegible]

- Catal 584
 Catalase 361, 362
 - in glycine degradation 397
 - in milk 689
 Catalysts of biological oxidations 402, 403
 Cataracts 450
 Catecholamines (see also *Adrenaline*, *Dopamine*, *Noradrenaline*) 730 sq.
 - assay 731
 - biosynthesis and release 731
 - in blood 731, 733
 - in cardiac infarction 623, 624
 - metabolism 731 sq.
 - in urine 668, 733
 Catechol O-methyltransferase in catechol-amine breakdown 731, 732
 Cathesins 410
 Cathepsin III. See *Leucine aminopeptidase*
 Cathepsin IV. See *Carboxypeptidase A*
 Cauliflower, amino acids 516
 - composition 503
 Caviar, composition 514
 Cavity ion dose 219
 Cb (columbium). See *Niobium*
 cc (centesimal second) 207
 cd (candela) 223
 Cd. See *Cadmium*
 CDP. See *Cytidine diphosphate*
 Ce. See *Cerium*
 Cefalotin, reference preparation 762
 Celery, composition 503
 Celiac disease in vitamin D deficiency 461
 Cell, metabolism 387, 388
 - protein, enzyme content 584
 Cellulose in intestinal mucosa 413
 Cellobiose 324
 Cellulose 326
 - in faeces 657, 659
 Celsius temperature scale 208, 209
 Cental 205
 Centesimal angle units 207, 208
 centi- (10⁻²) 9
 Centigrade temperature scale 208, 209
 Centimetre 200
 - reciprocal 213
 Centimetre-gramme-second (CGS) electro-magnetic and electrostatic units 215
 Cephalins 365, 375
 - in bile 655
 - in blood 604
 - in brain and spinal cord 520
 - in cerebrospinal fluid 638
 - in erythrocytes 604
 - formation 425
 - structure and hydrolysis 417
 Cephalothin, reference preparation 762
 Ceramide galactosides 376
 - glucosides in GAUCHER'S disease 377
 - lactoside 377
 Cereals, amino acids 516
 - composition 507, 508
 - vitamin losses in cooking 498
 Cereal products, composition 507, 508
 Cerebellar ataxia 452
 - hemispheres, enzyme activities 585
 Cerebral cortex, enzyme activities 585
 Cerebrum 372, 377
 Cerebronic acid 372
 - in phrenosin 377
 Cerebrose. See *D-Galactose*
 Cerebrosides 365, 376, 377
 - in brain and spinal cord 520
 - fatty acids of 369, 372
 - in erythrocyte sedimentation 559
 Cerebrospinal fluid 635 sq.
 - ammonia 449, 636
 - amount 525, 635
 - electrolytes 525, 636
 - insulin 736
 - isoleucine 449
 - leucine 449
 - pantothenic acid 488, 639
 - phenylalanine 448
 - thiamine 470, 639
 - valine 449
 Cerebrum, enzyme activities 585
 Cerium, flame lines 284
 - properties, isotopes, etc. 239
 Ceroid pigment formation, vitamin E in 466
 Cerotic acid 367
 - in waxes 377
 Ceruloplasmin. See *Caeruloplasmin*
 Caesium. See *Caesium*
 Cetoleic acid 369
 Cetyl alcohol in waxes 377
 Cf (californium) 248
 CGS (centimetre-gramme-second) electro-magnetic and electrostatic units 215
 ch (chain) 200
 ch (metric horsepower) 213
 Chain 200
 Chair conformation of steroids 378
 Chaldron 204
 Chard, composition 503
 CHE. See *Cholinesterase*
 Check-valve mechanism 542
 Cheese, composition 510
 Chenodeoxycholic acid, in bile 655, 656
 - in faeces 660
 - in plasma 601
 Cherries, composition 499
 Cherry-red spot 455, 456
 Chest circumference during growth 695 sq.
 Chestnuts, composition 507
 Chick antidermatitis factor. See *Pantothenic acid*
 Chicken, composition 512
 Chicory, composition 503
 Children (see also *Infants and Newborn*), ascorbic acid requirement 490
 - bile, amount 653
 - cholesterol 655
 - bile acids 656
 - blood, acetoacetic acid 608
 - acetone 608
 - alanine aminotransferase 594
 - amino acids 573, 574
 - ammonia 573
 - androgens 751
 - ascorbic acid 611
 - aspartate aminotransferase 593
 - borate 564
 - caeruloplasmin 593
 - carotenes 609
 - cholesterol 601, 603
 - copper 566
 - corticosteroids 745
 - creatine 572
 - creatinine 572
 - ergothioneine 573
 - fatty acids 601, 603
 - fructose diphosphate aldolase 599
 - galactose 1-phosphate 605
 - gases 570, 571
 - glucose 604, 605
 - glycerides 601, 603
 - glycerol 607
 - glycogen 606
 - growth hormone 720
 - haemoglobin 615, 617
 - β -hydroxybutyric acid 608
 - L-iditol dehydrogenase 590
 - iodine 564
 - iron 566
 - α -ketoglutaric acid 607
 - ketone bodies 608
 - lactate dehydrogenase 590
 - lipids 601, 603
 - magnesium 566
 - nonprotein nitrogen 572
 - pepsin 598
 - acid phosphatase 596
 - alkaline phosphatase 596
 - phosphate 563
 - inorganic phosphorus 563
 - potassium 564
 - proteins 579, 583
 - protoporphyrin 576
 - pyruvic acid 607
 - thyroid hormone 726
 - thyroxine breakdown 727
 - urea 572
 - uric acid 577
 - viscosity 558
 - vitamin A 609
 - vitamin D 461, 609
 - zinc 567
 - blood pressure 553, 554
 - blood volume 554, 555
 - BMR 539, 540
 - body surface area 528
 - nomogram 538
 - body weight. See under *Body weight*
 - bone age 706, 707
 - bone composition 521
 - bone growth, alkaline phosphatase and 585
 - epiphyseal 706 sq.
 - bone marrow cells 621
 Children, cerebrospinal fluid, leucocyte count 635
 - protein 637
 - corticosteroid secretion 743
 - dietary requirements 493 sq.
 - erythroblastosis 612
 - erythrocytes, count 614, 617
 - diameter 617
 - mean corpuscular haemoglobin 615
 - osmotic resistance 616
 - sedimentation rate 553
 - mean corpuscular volume 617
 - maximum expiratory flow rate 551
 - faeces, composition and properties 657 sq.
 - vitamin B₆ 473
 - gastric juice, acidity 643
 - pH value 647
 - secretion 647
 - normal measurements during growth 695 sq.
 - haematocrit 617
 - iodide metabolism 726
 - iodine requirements 497
 - leucocyte count 618, 619
 - lung values 550
 - nomograms 547
 - mineral requirements 486
 - nicotinic acid requirement 478
 - organ weights 710
 - appearance of ossification centres 706 sq.
 - pancreatic juice secretion 651
 - pernicious anaemia 485
 - pulmonary compliance 549, 552
 - pulmonary resistances 549, 552
 - reticulocytes 613
 - saliva, chloride 643
 - lactic acid 643
 - pH value 644
 - potassium 644
 - sodium 643
 - volume 643
 - sweat, acetylcholine 681
 - amino acids 680
 - electrolytes 679, 680
 - glucose 681
 - lactic acid 681
 - volume 679
 - teeth, composition 709
 - development 471
 - thiamine requirement 471
 - thrombocyte count 620
 - urine, N-acetylhistamine 670
 - acidity 662
 - amino acids 666, 667
 - amount 661
 - calcium 664
 - catecholamines 733
 - copper 664
 - corticosteroids 746 sq.
 - creatine 665
 - creatinine 665
 - erythropoietin 740
 - ethanolamine 663
 - fluoride 673
 - glucuronic acid 714
 - gonadotropins 735
 - insulin 665
 - nitrogen 756
 - oestrogens 674
 - organic acids 666
 - peptides 670
 - porphyrins 754
 - pregnanediol 669
 - tryptophan metabolites 676
 - vitamins 551
 - vital capacity 460
 - vitamin A deficiency 460
 - vitamin A poisoning 460
 - vitamin A requirement 475
 - vitamin B₆ requirement 464
 - vitamin D deficiency 461, 464
 - vitamin D poisoning 451
 - vitamin D requirement 451
 - water requirement 524
 Chi-squared distribution 166 sq.
 - significance limits 36 sq.
 Chitin 325
 Chitobiose in seminal plasma 684
 Chitosamine. See *D-Glucosamine*
 Chives, composition 504
 Chloride, in amniotic fluid 522
 - in bile 684
 - in blood 453, 562
 - in whole body 517, 518
 - in body fluids 523, 525
 - in bones 521
 - in cerebrospinal fluid 635

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- rate, conversion factors 274 sq, 523
 conversion factor into sodium chloride 251
 dietary requirements 496
 electrolyte balance 325
- chloride shift 562
 chloride, atomic weight multiples 253
 properties, isotopes, etc 255
 chloride 36, characteristics 292
 (*p*-Chlorobenzyl)cysteine in detoxication of
p-dichlorobenzene 445
 (*p*-Chlorobenzyl)glutathione in detoxica-
 tion of *p*-dichlorobenzene 445
 Chlorobenzylmercapturic acid in detoxica-
 tion of *p*-dichlorobenzene 445
 chlorogenic acid in coffee 509
 chlorophenol red indicator 283
 chlorophyll 362, 363
 chlorophyllase 363
 chlorotriamine, oestrogenic activity 735
 chlorotriamine, composition 509
 cholera 381
 Cholecalciferol See Vitamin D₃
 Cholelithiasis 739
 Choleglobin 360, 362
 Cholera agglutinating serum, reference
 reagent 764
 vaccines, reference preparations 757
 Cholera toxin 381
 Cholera toxin in faeces 660
 Cholesterol 5-en-3 β -ol See Cholesterol
 Δ^5 Cholesterol in faeces 660
 Cholesterol 374, 379
 - accumulation 476
 - adrenal steroids and androgens from 428, 429
 - in bile 655
 - biosynthesis 428, 429
 - inhibition by meclofenic acid 477, 478
 - in blood and spinal cord 458, 600, 601, 603, 604
 - in brain and spinal cord 520
 - in cerebrospinal fluid 638
 - degradation 401
 - in liver 426
 - in erythrocytes 600, 601
 - excretion in cerebrospinal fluid 638
 - in faeces 660
 - in foods 478 sq
 - in leucocytes 601
 - in lipoproteins 602
 - in milk 687
 - oestrogen synthesis from 431
 - in saliva 646
 - in semen 685
 - stereoisomerism 378
 - in synovial fluid 642
 - in thrombocytes 601
 - in tissues 522
 - in urinary acid ments 677, 678
 - in urine 675
 Cholesterol esterase 414
 Cholic acid in bile 655, 656
 activation of cholesterol esterase 414
 conjugation 609
 in faeces 601
 in plasma 492
 Choline 492
 activation 425
 in bile 654
 biosynthesis 434
 1- α -ketolysmethionine in 398
 in blood 375
 in liver cholin synthesis 425
- Choline, in lipids 365
 - in milk 683, 689
 - in phosphatidyl esters 375
 - in saliva 645
 - on semen 683
 - in urine 668, 674
- Chromic gonadotropin 715
 - - oestrogens and 757
 - growth-hormone prolactin 721
 - sac, development 691
 - thyrotropin, human 809
 Chromaffin granules 731
 Chromatophore hormone 721, 722
 Chromium, in blood 567
 - dietary requirements 497
 - flame tests 284
 - properties, isotopes, etc 236
 - in urine 654
 Chromium 51, characteristics 292
 - decay table 296
 - diagnostic use 289
 Chromogranin 731
 Chylomicrons 374
 - in serum 407, 408
 Chylomicronemia 659
 - in pancreatic juice 683
 Chylomicronogenesis 407
 - in pancreatic juice 652
 Ci (curie) 217
 Cinnamic acid, conjugation with glycine 444
 Circle, geometry 142
 Circulation, effect of catecholamines 734
 - action of corticosteroids 750
 - pulmonary 543, 544
 Cisterns See under Liver
 Cerebral fluid See Cerebrospinal fluid
 Catecholamines 386
 Cis-trans isomerism in phenylalanine 398
 - degradation 378
 Cis-trans isomerism, of fatty acids 373
 - of steroids 378
 Citrate, in blood 607
 - buffers 424
 - in cerebrospinal fluid 639
 - cleavage 424
 - fatty acid synthesis from 423
 - in foods 497 sq
 - formation 424
 - from glucose 420
 - in milk 687
 - poisoning 607
 - in saliva 645
 - in semen 685
 - in tricarboxylic acid cycle 390, 394
 - in urine 674
 - in yogurt 511
 Citrate (isocitrate) hydrolase See Aconitate
 hydratase
 Citrate-phosphate-borate buffer 280 eq
 Citric acid (or also Citrate) solutions, deci-
 normal 277
 - pH values 279
 Citric acid cycle See Tricarboxylic acid cycle
 Citron 491
 Citrovorum factor See 5 Formyltetrahydro-
 folic acid
 Circulation 449
 Circulation 334
 - in blood 445, 574
 - degradation 394, 395, 402
 - in sweat 689
 - in urea synthesis 442 sq
 Ci See Chloride and Chlorine
 Clams, composition 514
 Clearance See Renal clearance
 Clearance See Renal clearance
 Clostridial protease A in pancreatic juice 652
- Clostridium botulinum* antitoxins, standards 760
Clostridium oedematis toxoid, reference pre-
 paration 759
Clostridium welchii antitoxins, standards 761
 Clostridion acid 370
 Cm (curium) 248
 cm⁻¹ (reciprocal centimetre) 213
 CMP See Cytidine monophosphate
 Cobalt 213
 Co 1 See Nicotinamide-adenine dinucleotide
 Co 11 See Nicotinamide-adenine dinucleotide
 phosphate
 CoA See Coenzyme A
 CoASH See Coenzyme A
 CoA-transferase 386
 Cobalamins 482
 Cobalt, atomic weight multiples 230
 - in blood 566
- nine dinucleotides
 Coenzyme II See Nicotinamide ade-
 nine dinucleotide phosphate
 Cod liver oil, composition 510
 Codons 353
 Coeliac disease in vitamin D deficiency 461
 Coenaymas 382, 385
 - nucleotide 344 sq
 Coenzyme I See Nicotinamide adenine dinu-
 cleotide
 Coenzyme II See Nicotinamide adenine dinu-
 cleotide phosphate
 Coenzyme A (CoA, CoASH) 345, 488
 - in acetylation of amines 444
 - in ATP synthesis 404
- Coenzyme Q₁₀ 403, 406
 Coenzyme Q₁₀ in urine 676
 Coffee, composition 509
 Cohn fraction in lipoproteins 602
 Cola drink, composition 509

Index

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- Colistin, reference preparation 762
 - standard 761
 Collagen, biosynthesis, ascorbic acid in 490
 - metabolism, hydroxyproline excretion and 666
 - in tissues 522
 Collagen diseases, salivary secretion in 643
 Collagen hydroxyproline 432
 Colloid-osmotic pressure of plasma 526, 558
 Colonic mucosa, respiratory rate 387
 Colostrum, composition 687 sq.
 - fatty acids 687
 Colour index of blood 615
 Colour vision, plates for testing ... (inside back cover)
- Columbium. See Niobium
- Commutative law 132
- Compliance, respiratory 545, 552
 - in children, determination 549
- Compound A. See 11-Dehydrocorticosterone
- Compound B. See Corticosterone
- Compound E. See Cortisone
- Compound F. See Cortisol
- COMT (catechol O-methyltransferase) in catecholamine breakdown 731, 732
- Concentration units 226, 227, 271
 - conversion of 251
- Condensing enzyme in tricarboxylic acid cycle 390, 391
- Conductance, pulmonary 546
- Conductivity, electric 216
- Cone, geometry 142
- Cone vision 223
- Confectionery, composition 509
- Confidence limits 150, 152, 154 sq.
 - tables 43, 63, 85 sq.
- Congo red indicator 283
- Conjunctival xerosis 460
- Connective tissue, effect of growth hormone - respiratory rate 387
- Conn's syndrome. See Hyperaldosteronism
- Constants, atomic 228, 229
 - field 228
 - mathematical 9
 - physical 228 sq.
 - thermodynamic 228
- Constitution. See Body type
- Contact therapy with radionuclides 290
- Contractile tissue, effect of oxytocin and vasopressin 723, 724
- Cooley's anaemia 448
 - trait 448
- Coombs' test 626
- Coordinated Universal Time 207
- COP (colloid-osmotic pressure) of blood 526, 558
- Copper, in amniotic fluid 522
 - atomic weight multiples 250
 - in bile 654
 - in biological oxidations 403
 - in blood 566
 - in whole body 517
 - in bones 521
 - in cerebrospinal fluid 636
 - dietary requirements 496
 - in erythrocytes 566
 - in faeces 658
 - flame lines 284
 - in foods 499 sq.
 - in gastric juice 649
 - in hair and nails 520
 - in milk 688
 - in organs 519
 - in pancreatic juice 652
 - in placenta 522
 - properties, isotopes, etc. 236
 - in saliva 645
 - in semen 683
 - in skin 520
 - in sweat 680
 - in synovial fluid 641
 - in teeth 521
 - in urate oxidase 419
 - in urine 664
 - in erythrocytes 566
- Copper-64, characteristics 292
 - decay table 298, 299
 - gamma ray constant 221
- Copper oxide, decinormal solutions 277
- Copper sulphate, decinormal solutions 277
- Coproporphyrin, idiopathic 355, 357, 358
- Coproporphyrins 575
 - in blood 659
 - in faeces 670
 - in urine 454
- Coproporphyrin I, accumulation 654
 - in bile 654
- Coproporphyrin I, biosynthesis 454
 - in urine 670
- Coproporphyrin III, in bile 654
 - in haem synthesis 454
 - in urine 455, 670
- Coproporphyrinogens 356, 357
- Coproporphyrinogen I, biosynthesis 454
- Coproporphyrinogen III in haem synthesis 454
- Coprosterol in faeces 660
- Cord (unit) 203
- Cord blood, alanine aminotransferase 594
 - amino acids 573
 - aspartate aminotransferase 593
 - bases 571
 - bicarbonate 571
 - bilirubin 576, 577
 - bradykinin 742
 - caeruloplasmin 593
 - calcium 565
 - carbon dioxide 570, 571
 - carotenes 609
 - chloride 562
 - cholesterol 603
 - cholinesterase in 595
 - citric acid 607
 - copper 566
 - coproporphyrin 575
 - corticosteroids 745
 - creatine kinase 594
 - creatinine 572
 - ergothioneine 573
 - erythroblasts 612
 - erythrocyte count 614
 - erythrocyte osmotic resistance 616
 - erythropoietic activity 740
 - fatty acids 601, 603
 - folic acid 610
 - fructosediphosphate aldolase 599
 - galactose 1-phosphate 605
 - glucose 604
 - glucosylphosphate isomerase 600
 - growth hormone 720
 - haematocrit 614
 - haemoglobin 576, 615
 - α -hydroxybutyrate dehydrogenase 591
 - L-iditol dehydrogenase 590
 - insulin 736
 - iodine 564
 - iron 566
 - isocitrate dehydrogenase 591
 - α -ketoglutaric acid 607
 - lactate dehydrogenase 590
 - lactic acid 607
 - lecithin 604
 - lipids 603
 - magnesium 566
 - malate dehydrogenase 591
 - nonprotein nitrogen 572
 - oestrogens 756
 - oxygen 570
 - alkaline phosphatase 596
 - phosphoethanolamine 573
 - pH value 560
 - placental lactogen 721
 - potassium 564
 - progesterone and metabolites 754
 - proteins 583
 - protoporphyrin 576
 - pyruvic acid 607
 - riboflavin 609
 - sodium 565
 - thrombocyte count 620
 - tocopherols 609
 - urea 572
 - vitamin A 609
 - vitamin B₆ 609
 - vitamin B₁₂ 610
 - zinc 567
- Cort ester. See D-Glucose 1-phosphate
- Corn, sweet (maize), composition 504
- Cornflakes, composition 508
- Corn flour, composition 508
- Corn oil, composition 510
- Cornstarch, composition 508
- Corn sugar. See D-Glucose
- Corpuscular haemoglobin. See under Erythrocytes
- volume. See Erythrocyte volume
- Corpus luteum, progesterone secretion 753
- Corpus luteum-ripening hormone. See Luteinizing hormone
- Correlation coefficient 179 sq.
 - tables 61 sq.
- Corrinoids 482 sq.
- Cortex, adrenal. See Adrenal cortex
- bone, composition 521
- Cortexolone. See 11-Deoxycortisol
- Cortexone. See Deoxycorticosterone
- Corticosteroids 381, 742 sq.
 - regulation of ACTH secretion 717
 - assay 743, 744
 - biological activity 748 sq.
 - biosynthesis 426, 428 sq.
 - effect of ACTH 717
 - inborn defects 456
 - rates 743, 745
 - in blood 745
 - in cardiac infarction 624
 - serum dehydroascorbic acid and 611
 - 17-deoxy-, structure and assay 744
 - in urine 746
 - glucocorticoids. See Glucocorticoids
 - 11-hydroxy-, structure and assay 744
 - in urine 747
 - 17-hydroxy-, structure and assay 744
 - in plasma 745
 - excretion during pregnancy 749
 - 17-ketogenic, structure and assay 744
 - in urine 746 sq.
 - metabolism 428 sq., 430, 746, 747
 - inborn errors 456
 - mineralocorticoids. See Mineralocorticoids
 - reducing, in plasma 745
 - structure and assay 744
 - in urine 430, 746 sq.
 - Corticosteroid-binding globulin 745
- Corticosterone 379, 743 sq.
 - in adrenals 743
 - biological activity 749
 - biosynthesis 428, 429
 - rates 743
 - in blood 745
 - protein binding 428
 - breakdown 746, 747
 - release, effect of ACTH 717
 - in urine 747
- Corticotrophic hormone. See Corticotropin
- Corticotropin (ACTH) 716, 717
 - effect on adrenal cortex 430
 - testing of adrenocortical function 747
 - effect on androgen formation 751
 - in cardiac infarction 624
 - in catecholamine secretion 731
 - and haemorrhagic diatheses 623, 624
 - and melanotropins 721
 - releasing factors 717, 722, 723
 - secretion, effect of vasopressin 723
 - standard 762
- Cortisol 379, 742 sq.
 - regulation of ACTH secretion 717
 - in adrenals 749
 - biological activity 749
 - biosynthesis 428, 429
 - rates 743, 745
 - in blood 716, 745
 - protein binding 428
 - breakdown 746, 747
 - and haemorrhagic diatheses 623, 624
 - release, effect of ACTH 717
 - in urine 430, 747
- Cortisone 379, 742 sq.
 - in adrenals 743
 - biological activity 749
 - biosynthesis 428, 429
 - rates 746, 747
 - breakdown 623, 624
 - and haemorrhagic diatheses 623, 747
 - in urine 430, 747
- α -Cortol 379
 β -Cortol 379
 α -Cortolone 379
 β -Cortolone 747
 Cortolones in urine 139
 cos (cosine) 139
 Cosine 138, 139
 cot (cotangent) 138, 139
 Cotangent 510
 Cottonseed oil, composition 216
- Coulomb
- Cow's milk. See under Milk
- Coxsackie virus antisera, reference reagents. Cozymase. See Nicotinamide-adenine dinucleotide
- Cp (cassiopeium) 241
- CPK (creatine phosphokinase). See Creatine kinase
- Cr. See Chromium
- Crab, composition 514

A detailed index to the statistical tables (pages 28-131) and chapters on Statistical Methods (pages 146-196) will be found on pages 197-198.

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Index.

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- hydroxymethylcytidine monophosphate (dHMCMP) 343
- Deoxyinosine 341
- 21-Deoxyketols, structure and assay 744
- excretion during pregnancy 749
- 6-Deoxy-L-mannose 313
- Deoxy-5-niethylcytidine monophosphate (dMCMF) 343
- Deoxymyoglobin. See Myoglobin
- Deoxypentoses, degradation 399
- Deoxypyridoxine 474
- Deoxyribonucleases in pancreatic juice 652
- Deoxyribonuclease I 406, 418
- in plasma 597
- Deoxyribonuclease II 406, 418
- in plasma 597
- Deoxyribonuclease 3'-nucleotidohydrolase. See Deoxyribonuclease II
- Deoxyribonucleic acid oligonucleotidohydrolase. See Deoxyribonuclease I
- Deoxyribonucleic acid (DNA) 351 sq.
- biosynthesis 351, 352
- folic acid in 479
- vitamin B₁₂ in 485
- enzymatic cleavage 406
- depolymerization 418
- in leucocytes 578
- in semen 684
- viral, synthesis 352
- Deoxyribonucleoprotein 351
- Deoxyribosyladenine, formation, vitamin B₁₂ in 485
- 2-Deoxy-D-ribose 313
- formation from glucose 420
- phosphates 318
- 1-phosphate, formation from nucleosides 339, 340
- 5-phosphate, degradation 399
- Deoxyribosyladenine. See Deoxyadenosine
- Deoxyribosylcytosine. See Deoxycytidine
- Deoxyribosylguanine. See Deoxyguanosine
- Deoxyribosylhypoxanthine 341
- Deoxyribosylthymine. See Deoxythymidine
- Deoxyribosylxanthine 341
- 21-Deoxysteroids, excessive synthesis 456
- Deoxythymidine 340
- diphosphate (dTDP) 343
- monophosphate (dTMP) 343, 438, 439
- in DNA 351
- formation 438, 439, 479
- triphosphate (dTTP) 343
- Deoxythymidyllic acid. See Deoxythymidine monophosphate
- Deoxyuridylic acid in pyrimidine synthesis 439
- Deoxyxanthosine 341
- Dephospho-coenzyme A in coenzyme A formation 487
- Depot fats 374
- Dermatan sulphate 326
- Dermatitis, photosensitive 452
- Dermatomes of primary rami of spinal nerves (inside back cover)
- Desmosterol in cholesterol synthesis 426, 427
- Desoxy-. See Deoxy-
- Desulphhydrases, vitamin B₆ and 475
- Detoxication mechanisms 442 sq.
- Deuterium, properties 234
- oxide, density 230
- Deuteroporphyry 358
- in faeces 659
- Dexamethasone 379
- regulation of ACTH secretion 717
- testing of adrenocortical function 747
- relative biological activity 750
- Dextran 327
- as plasma expanders 530
- Dextrins, enzymatic hydrolysis 411, 412
- α -limit, from starch 411
- Φ -Dextrin 411
- Dextrin-1,6-glucosidase 412
- deficiency 450, 451
- Dextrinosis, limit 451
- Dextro compounds 308, 309
- Dextronic acid. See D-Gluconic acid
- Dextrose. See D-Glucose
- dGDP (deoxyguanosine diphosphate) 343
- dGMP. See Deoxyguanosine monophosphate
- dGTP (deoxyguanosine triphosphate) 343
- DHF. See Dihydrofolic acid
- dHMCMP (deoxy-5-hydroxymethylcytidine monophosphate) 343
- Diabetes, galactose 450
- gastric juice secretion 647
- from destruction of hypothalamus 723
- Diabetes, urinary 1-methyl-2-pyridone 5-carboxylamide 676
- blood thiamine 609
- Diabetes insipidus 452, 453
- fluid deprivation test in 535
- 5-N,O-Diacetylneuraminic acids 316
- Diacylglycerols. See Diglycerides
- Diamines in semen 684
- Diaminobiotin 487
- α,ϵ -Diamino-*n*-caproic acid. See L-Lysine
- α,ϵ -Diamino- δ -hydroxy-*n*-caproic acid 331
- α,ϵ -Diaminopimelic acid, decarboxylation 394
- Di-[α -aminopropionic]- β -disulphide. See Cystine
- 2,5-Diamino-*n*-valeric acid. See L-Ornithine
- Diaminoxidase, vitamin B₆ and 475
- Diammonium hydrogen phosphate solutions, pH values 279
- 1,3-Diazine. See Pyrimidine
- Dibucaine number 595
- p*-Dichlorobenzene, mercapturic acids from 445
- Dicumarol, vitamin K and 467
- Diego blood-group system 632
- clinical significance 633
- Dienoestrol, oestrogenic activity 755
- Dietary allowances 493 sq.
- tables 498 sq.
- Diethylstilboestrol, oestrogenic activity 755
- Diethyl sulphide in urine 663
- Diffusing capacity of lungs 545, 552
- Diffusion constants of plasma proteins 580
- Digestion 389
- Digestive enzymes 405 sq.
- Digitalis, standard 763
- D*-Digitoxose 313
- Diglycerides 365, 374
- in bile 655
- in faeces 659
- in serum 601
- in triglyceride synthesis 426
- Dihydrocholesterol in serum 601
- Dihydro-compounds 381
- 22-Dihydroergosterol 462
- vitamin D from 461
- Dihydrofolic acid (DHF), biosynthesis 478
- in pyrimidine synthesis 439
- reduction to tetrahydrofolic acid 437
- Dihydro-*orotate* in pyrimidine synthesis 439
- Dihydro-*orate* dehydrogenase in pyrimidine synthesis 439
- Dihydro-*orotic* acid in pyrimidine synthesis 439
- Dihydropterotic acid in folic acid synthesis 478
- Dihydropteroylglutamic acid. See Dihydrofolic acid
- Dihydrospingosins, in lipids 365
- in sphingolipids 376
- Dihydrostreptomycin, standard 761
- Dihydrothymine in thymine degradation 401
- Dihydrouracil in degradation of cytosine and uracil 401
- Dihydroxyacetone 311, 313
- phosphate 317
- in carbohydrate synthesis and breakdown 441
- in erythrocytes 605
- in glucose 6-phosphate formation 422
- in glycerophosphates from 420
- in glycolysis 389
- in lactic acid fermentation 390
- erythro-trans*-1,3-Dihydroxy-2-amino-octadec-4-ene. See Sphingosine
- Dihydroxycholine acids in plasma 601
- Dihydroxycholesterols in synthesis of adrenal steroids and androgens 428, 429
- D*-(+)-*N*-(α,γ -Dihydroxy- β -dimethylbutyryl)- β -alanine. See Pantothenic acid
- 5,6-Dihydroxyindole in melanin formation 440
- 11 α ,15-Dihydroxy-9-ketoprost-5,13-dienoic acid 373
- 11 α ,15-Dihydroxy-9-ketoprost-5,13,17-trienoic acid 373
- 11 α ,15-Dihydroxy-9-ketoprost-13-enoic acid 373
- 17,21-Dihydroxy-20-ketosteroids in urine 746
- 3,4-Dihydroxymandelic acid, from catecholamine breakdown 732
- in urine 675
- 2,6-Dihydroxy-5-methylpyrimidine. See Thymine
- 3,4-Dihydroxy- β -phenylacetaldehyde from catecholamine breakdown 732
- 3,4-Dihydroxyphenylacetic acid, from catecholamine breakdown 732
- in urine 675
- 3,4-Dihydroxyphenylalanine (dopa), in adrenal and noradrenaline formation 440
- 3,4-Dihydroxyphenylalanine, decarboxylation 394
- in melanin formation 440
- 3,4-Dihydroxy- β -phenylethanol from catecholamine breakdown 732
- 3,4-Dihydroxyphenylethylamine (dopamine) 730
- in adrenal and noradrenaline formation 440
- breakdown 732
- formation from 3,4-dihydroxyphenylalanine 394
- hydroxylation, ascorbic acid in 490
- in urine 668, 733
- 3,4-Dihydroxyphenylglycol from catecholamine breakdown 732
- 3,4-Dihydroxyphenylglycolaldehyde from catecholamine breakdown 732
- 17 α ,21-Dihydroxypregna-1,4-diene-3,11,20-trione. See Prednisone
- 3 α ,20 α -Dihydroxy-5 α -pregnane. See α -Allo-pregnadiol
- 3 β ,20 α -Dihydroxy-5 α -pregnane 379
- 3 α ,21-Dihydroxy-5 β -pregnane-11,20-dione 380
- 11 β ,21-Dihydroxypregna-4-en-18-al-3,20-dione. See Aldosterone
- 11 β ,17 α -Dihydroxypregna-4-ene-3,20-dione 379
- 11 β ,21-Dihydroxypregna-4-ene-3,20-dione. See Corticosterone
- 17 α ,21-Dihydroxypregna-4-ene-3,20-dione. See 11-Deoxycortisol
- 17 α ,21-Dihydroxypregna-4-ene-13,11,20-trione. See Cortisone
- 2,3-Dihydroxypropanal. See D-Glycerinaldehyde
- 1,3-Dihydroxypropan-2-one. See Dihydroxyacetone
- D*-(α,β -Dihydroxypropionic acid. See D-Glyceric acid
- 2,6-Dihydroxypurine. See Xanthine
- 2,6-Dihydroxypyrimidine. See Uracil
- 2,6-Dihydroxypyrimidine-4-carboxylic acid. See Orotic acid
- 3,5-Di-iodo-3'-methyl-DL-thyronine, comparative potency 727
- 3,5-Di-iodo-L-thyronine, comparative potency 727
- L-3,5-Di-iodotyrosine 330, 726
- peptide-linked, in thyroid hormone formation 440
- Diketohydrindylidenediketohydrindamine 329
- Dimercaprol, reference preparation 763
- N*⁴,*N*⁶-Dimethyladenosine 354
- Dimethylallyl pyrophosphate in cholesterol synthesis 426, 427
- Dimethylamine, in blood 573
- in urine 668
- p*-Dimethylaminoozobenzene indicator 283
- Dimethylaminooethylamine buffer 280 sq.
- N*-Dimethylaminoleucylglycine buffer 280 sq.
- 5,6-Dimethylbenzimidazole riboside in vitamin B₁₂ synthesis 484
- 5,6-Dimethylbenzimidazolylalquo-cobamide 482, 483
- 5,6-Dimethylbenzimidazolylcyanocobamide. See Vitamin B₁₂
- 5,6-Dimethylbenzimidazolylhydroxocobamide 482, 483
- 7,8-Dimethyl-10-(*o*-duleityl)isalloxazine 472
- Dimethylglutamic acid buffer 280 sq.
- N*²,*N*²-Dimethylguanosine 354
- 7,8-Dimethyl-10-(*o*-ribityl)isalloxazine. See Riboflavin
- 5,6-Dimethyl-1-(α -ribofuranosyl)benzimidazole 3'-phosphate 363
- 5,8-Dimethyltolcol 465
- 7,8-Dimethyltolcol 465
- 5,8-Dimethyltocotrienol 465
- 7,8-Dimethyltocotrienol 465
- N,N*-Dimethyltryptamine, in blood 575
- in urine 669
- Dinitrophenol indicators 408, 409
- Dipectidases 468
- Dipeptides, enzymatic hydrolysis 386
- Dipeptide hydrolases 448
- o*-Diphenol oxidase, in albinism 503
- caeruloplasmin and 503
- 1,3-Diphosphoglycerate (*o*-glyceric acid 1,3-diphosphate) 317
- in carbohydrate synthesis and breakdown 416
- enzymatic cleavage 603
- in erythrocytes 389
- in glycolysis 523
- Diphosphomositides in brain and spinal cord 523
- Diphosphopyridine nucleotide. See Nicotinamide-adenine dinucleotide
- Diphtheria antitoxins, standards 701, 701

A detailed index to the statistical tables (pages 28–131) and chapter on Statistical Methods (pages 146–196) will be found on pages 197–198.

Diphtheria antitoxins, isoforms, standards	759	$\Delta^{11,12,13}$ Eicosatetraenoic acid See Arachidonic acid	Enzymes, digestive	405 sq
Distance modulus	201		- in salivary	645
Daitemper anisum, standard	761		- in semen	684
Distributive law	132		- in sweat	681
Diuretics, effect on enzyme excretion	632		- in synovial fluid	641
- osmotic	533		- in tissues	585, 586
Diuretic test	747		- tissue-specific	584
dk (deks, 10 ³)	9		- units	584
dNMP (deoxy-3 methylcytidine mono-phosphate)	343	- action of corticosteroids	- in urine	672 sq
DNA See Deoxyribonucleic acid			Eosinopenia	620
DNAse See Deoxyribonuclease			Eosinophils, in blood	619, 620
DNA nucleosyltransferase	351		- in bone marrow	621
DNA polymerase	351		- action of corticosteroids	750
Dxase See Deoxyribonuclease			- dimensions	618
DOC See Drosyoptocortisone			Eosinophil test See Thomas's test	
Docosanoic acid	367	- moment	Eosinophilia	620
$\Delta^{11,12,13}$ Docosapentaenoic acid	370	- radiation units	Ephedra	206, 207
Δ^{11} Docosenoic acid	369	- units	Ephedrine	379
Δ^{11} Docosenoic acid	369		- in urine	746
trans- Δ^{12} Docosenoic acid	369		Epidermis See Skin	
13 Docosenoic acid	371			
Dodecanoic acid See Lauric acid				
Δ^1 Dodecenoic acid	368			
Δ^1 Dodecenoic acid	368			
Δ^1 Dodecenoic acid	368			
Dodecenoic acids in milk	637			
Dombrock blood group system	632			
Depe See 3,4 Dihydroxyphenylalanine				
Deps decarboxylase in adrenalin and noradrenalin formation	440			
Dopsamine See 3,4 Dihydroxyphenylalanine				
Dopsamine hydroxylase in adrenalin and noradrenalin formation	440			
Dose equivalent of radiation	221			
Dosimetry of radionuclides	217 sq, 286, 287			
Dotsentanoic acid See Lactonic acid				
dpm (disintegrations per minute)	217			
DPN (diphosphopyridine nucleotide) See Nicotinamide adenine dinucleotide				
dps (disintegrations per second)	217	- multiples		
dr (dram, drachm)	205	- in human body	234 sq, 517 sq	
Drethm	205	- electronic configurations	249	
- fluid	204	- contents in foods	498 sq	
Drm	205	- periodic system	231	
- epithelial	205	- properties, isotopes, etc	234 sq	
- fluid	204	Elementary charge	223	
Drying pressure, vessel	544	α Eleosteic acid	370	
Drops per minute, nomogram	529	Ellipse, geometry	142, 144	
Dry measures	204	Ellipocytosis	614	
dry pt (dry part)	204	Em (emanation)	244	
dry qt (dry quart)	204	Eman	217	
DTDP (deoxythymidine diphosphate)	343	Embryo (<i>see also</i> Fetus), hargoglobin	244	
dTMP See Deoxythymidine monophosphate		- lactic acid fermentation	615	
dTTP (deoxythymidine triphosphate)	343	- size and weight	388	
Dubin Johnson syndrome	454	emu (electromagnetic units)	691, 692	
- serum bilirubin	577	Enanthic acid	218, 219	
Duck, composition	512	Enanthic acid	366	
Duffy blood group system	632	Endives, composition	594	
- clinical significance	633	Endocrine organs, weights	710	
Duodenal ulcer, gastric juice secretion	647	Endopeptidases	405 sq	
Dwarfs	449, 453	Energy dose of radionuclides	218, 286, 287	
- pituitary	720	- electronic	216	
- and ossification	707	- fluence of radiation	218	
- premenstrual and ossification	707	- flux density of radiation	218, 221	
dwt (pennweight)	205	- mechanical units and symbols	212, 213	
Dy See Dyspepsia		- metabolism (<i>see also</i> Calorimetry)	387 sq	
dyn (dyne)	211	Energy supplying reactions	389 sq	
Dyne	211	ENO (enolase) See Phosphopyruvate hydratase		
Dysentery anisum, standard	760			
Dyspepsia, flame lines	284			
- properties isomers etc	240			
E (base of natural logarithms)	132			
Earth's crust, composition	234 sq			
EC numbers of enzymes	384, 386			
Ectopic sweat See Sweat				
Ectopic sweat reference resins	764			
Eel, composition	514	- allotropic	382	
Egg amino acids	316	- in bile	655	
- composition	510, 511	- in biological oxidations	402, 403	
- vitamin losses in cooking	498	- in blood	584 sq	
Eggplant, composition	504	- elevation	586	
Egg powder, composition	511	- in cell proteins	384	
Eicosanoic acid See Arachidic acid		- in cerebrospinal fluid	638	
$\Delta^{11,12,13}$ Eicosapentaenoic acid	370	- classification and numbering	385, 386	
		- congenital defects	446 sq	
		- diagnostic use	386 sq	

- Erythrocytes (*cont'd*), count (RBC) . . . 613, 614, 617
 - creatine . . . 572
 - creatinine . . . 572
 - dihydroxyacetone phosphate . . . 605
 - dimensions . . . 613, 614, 617
 - diphenylglyceric acid . . . 605
 - dry substance . . . 561
 - surface density of electric charge . . . 560
 - electrophoretic mobility . . . 560
 - enzymes . . . 585
 - - allotypy . . . 634
 - ergothioneine . . . 573
 - ethanolamine . . . 573
 - fatty acids . . . 600, 601
 - folic acid . . . 479, 610
 - fructose 1,6-diphosphate . . . 605
 - fructose 6-phosphate . . . 605
 - galactose 1-phosphate . . . 605
 - glucose . . . 604
 - glucose 6-phosphate . . . 605
 - glucuronic acid . . . 605
 - glutathione . . . 573
 - glyceraldehyde 3-phosphate . . . 605
 - glycogen . . . 606
 - glycolipids . . . 377
 - glycoproteins . . . 606
 - mean haemoglobin concentration 576, 615, 617
 - mean haemoglobin content . . . 615, 617
 - haemoglobin iron . . . 566
 - haemolysis. See Haemolysis
 - lactic acid . . . 607
 - lactic acid fermentation . . . 388
 - lecithin . . . 604
 - lifetime . . . 616
 - lipids . . . 600, 601
 - lipid phosphorus . . . 563
 - lysolcithin . . . 604
 - magnesium . . . 566
 - manganese . . . 567
 - metabolism . . . 616
 - 5-methyltetrahydropteroylglutamic acid . . . 479
 - molybdenum . . . 567
 - nitrogen . . . 572
 - nonprotein nitrogen . . . 572
 - nucleotide pentose . . . 605
 - octulose 1,8 diphosphate . . . 605
 - osmotic resistance . . . 616
 - pentose 5-phosphate . . . 605
 - pH value . . . 560
 - phosphatides . . . 601, 604
 - phosphoenolpyruvic acid . . . 605
 - phosphoglyceric acids . . . 605
 - phosphoric esters . . . 563
 - phosphorus . . . 563
 - plasmalogen . . . 604
 - polychromatic. See Reticulocytes
 - porphobilinogen . . . 575
 - porphyrins . . . 357, 358
 - potassium . . . 564
 - precursors . . . 612
 - proteins . . . 579
 - protein nitrogen . . . 572
 - protoporphyrin . . . 455, 576
 - pterins . . . 610
 - purine nucleoside phosphorylase . . . 418
 - pyrophosphatase . . . 416
 - pyruvic acid . . . 607
 - respiratory rate . . . 387
 - riboflavin . . . 471, 473, 609
 - sedimentation mechanism . . . 559
 - sedimentation rate (ESR) . . . 558, 559
 - sedoheptulose 1,7 diphosphate . . . 605
 - sickle-cell . . . 614
 - - sedimentation . . . 559
 - sodium . . . 565
 - specific gravity . . . 557
 - specific heat . . . 560
 - sphingomyelin . . . 604
 - sugar phosphates . . . 605
 - sulphur . . . 563
 - in synovial fluid . . . 640
 - in thalassaemias . . . 446
 - thiamine . . . 470, 609
 - triglycerides . . . 601
 - triosephosphate . . . 605
 - urea . . . 572
 - uric acid . . . 577
 - in urine . . . 661, 677
 - uroporphyrin . . . 576
 - vital-granulated. See Reticulocytes
 - vitamin B₁₂ . . . 609
 - vitamin B₁₂ . . . 610
 - volume . . . 554 sq., 613
 - - gain in pregnancy . . . 691
 Erythrocytes, volume, mean (mean corpus-
 cular volume) . . . 614, 615, 617
 - - nomogram . . . 556
 - - tracer study . . . 289
 - water . . . 561
 - weight gain in pregnancy . . . 690
 - zinc . . . 567
 Erythrocyte count (RBC) . . . 613, 614, 617
 Erythrocyte sedimentation rate (ESR) . . . 558, 559
 Erythrodontia . . . 454
 Erythromycin, standard . . . 761
 D-Erythropentulose. See D-Ribulose
 Erythropoiesis, riboflavin and . . . 472
 Erythropoietin . . . 740
 - reference preparation . . . 763
 - riboflavin and . . . 472
 D-Erythrose . . . 310, 313
 - 4-phosphate . . . 317
 - in pentose phosphate cycle . . . 421, 422
 D-Erythrulose . . . 311
 L-Erythrulose . . . 313
 - 1-phosphate . . . 317
 Es (einsteinium) . . . 248
 ESR (erythrocyte sedimentation rate) . . . 558, 559
 Essential amino acids, dietary requirements . . . 496
 - fatty acids. See under Fatty acids
 Esterases . . . 405
 - allotypy . . . 634
 - in bile . . . 655
 - in cerebrospinal fluid . . . 638
 - in vitamin A metabolism . . . 457
 Ester hydrolases. See Esterases
 Estr-. See Oestr-
 esu (electrostatic units) . . . 215, 216
 Ethanoic acid. See Acetic acid
 Ethanol, in blood . . . 606
 - calorific value . . . 509, 526
 - intoxication, serum enzyme changes . . . 586
 Ethanolamine, in blood . . . 573, 574
 - in cephalin synthesis . . . 425
 - in cerebrospinal fluid . . . 637
 - formation from serine . . . 394
 - in leucocytes . . . 573
 - in lipids . . . 365
 - in phosphatidyl esters . . . 375
 - in urine . . . 668
 Ethinyl-. See Ethynyl-
 β -Ethylacetyl-coenzyme A in norleucine
 degradation . . . 396
 Ethyl alcohol. See Ethanol
 24-Ethyl-5 α -cholestane in steroids . . . 381
 17 α -Ethyl-17 β -hydroxy-19-norandrost-4-en-
 3-one . . . 380
 17 α -Ethynyl-17 β -hydroxy-19-norandrost-
 4-en-3-one . . . 380
 17 α -Ethynyl-17 β -hydroxyoestr-5(10)-en-
 3-one . . . 380
 Ethynylloestradiol . . . 380
 - oestrogenic activity . . . 755
 17 α -Ethynylloestra-1,3,5(10)-trien-3,17 β -
 diol. See Ethynylloestradiol
 Etio-. See Actio-
 Eu. See Europium
 Euglobulinolysis time . . . 625
 EULER numbers . . . 9
 EULER's constant . . . 9
 Europium, flame lines . . . 284
 - properties, isotopes, etc. . . 240
 eV (electron volt) . . . 213
 EVANS' growth test . . . 719
 Exchange transfusions, serum bilirubin as
 guide to . . . 577
 Exocytosis . . . 731
 Exopeptidases . . . 405, 408 sq.
 Exophthalmos-producing substance . . . 718
 Expiratory flow rate, maximum (MEFR) . . . 543
 - nomograms . . . 550
 - values . . . 551
 - reserve volume . . . 541, 550
 - volume, forced (FEV) . . . 543
 - - determination . . . 548, 549
 Exponents . . . 132
 Exponential equations . . . 137, 138
 - functions . . . 16, 17
 Extracellular fluid, total volume . . . 518, 523
 - gain in pregnancy . . . 690
 Extrinsic system in blood coagulation . . . 622, 625
 F
 f (femto-, 10⁻¹⁵) . . . 9
 F (farad) . . . 216
 F. See Fluorine
 °F (degree Fahrenheit) . . . 209
 FA. See Folic acid
 Factor A (2-methyladeninecyano cobamide) . . . 483
 Factor B (actinocobalamin) . . . 483
 Factor III (5-hydroxybenzimidazolyl-
 cyano cobamide) . . . 483
 Factors I-XIII (blood coagulation) . . . 622 sq.
 Factorials . . . 135, 136
 - logarithms . . . 26, 27
 FAD. See Flavin adenine dinucleotide
 Faeces (*see also* Stools) . . . 657 sq.
 - electrolytes . . . 525, 658
 - fatty acids . . . 371, 660
 - glucose and galactose . . . 452
 - porphyrins . . . 358
 - porphyrin excess . . . 455
 - plasma proteins . . . 289, 659
 - thyroxine . . . 727
 - vitamin B₁₂ . . . 475, 660
 - water loss in . . . 524, 657
 Fahrenheit temperature scale . . . 208, 209
 FANCONI syndrome . . . 452, 453
 - in vitamin D deficiency . . . 464
 FAO/WHO reference protein . . . 516
 Farad . . . 216
 FARADAY constant . . . 228
 Farnesyl pyrophosphate in cholesterol
 synthesis . . . 426, 427
 Fasting, blood, glucose . . . 604
 - growth hormone . . . 719
 - ketone bodies . . . 608
 - gastric juice, acidity . . . 648
 - volume . . . 647
 - ketone body excretion . . . 674
 Fats (*see also* Lipids and Triglycerides) . . . 365, 374 sq.
 - absorption, transport, storage . . . 374
 - contribution to BMR . . . 539
 - in whole body . . . 517
 - gain in pregnancy . . . 690
 - in cerebrospinal fluid . . . 638
 - depot . . . 374, 495
 - dietary, composition . . . 510
 - effect on blood coagulation . . . 622
 - effect on depot fat . . . 374
 - in foods . . . 498 sq.
 - requirements . . . 495
 - enzymes attacking . . . 405
 - in faeces . . . 657, 660
 - metabolism . . . 391 sq.
 - water from . . . 524
 - in milk . . . 687, 689
 - neutral. See Triglycerides
 fath (fathom) . . . 200
 Fathom . . . 200
 Fatty acids . . . 366 sq.
 - activation . . . 425
 - in bile . . . 655
 - biosynthesis . . . 420, 424, 425
 - pentose phosphate cycle and . . . 422
 - in blood . . . 600, 601, 603, 604
 - breakdown . . . 391 sq., 402
 - in formation of cephalin . . . 425
 - in cerebrospinal fluid . . . 638
 - in erythrocytes . . . 600, 601
 - essential . . . 373, 492
 - dietary requirements . . . 495
 - in faeces . . . 659, 660
 - in depot fat . . . 374
 - in foods . . . 498 sq.
 - hydroxamic acids from . . . 425
 - in formation of lecithin . . . 687
 - in milk . . . 685
 - in spermatozoa . . . 373
 - symbols . . . 466
 - unsaturated, oxidation, vitamin E in . . . 675
 - in urine . . . 404, 414
 Fatty acid ester hydrolases . . . 404, 414
 Fatty acyl-coenzyme A. See Acyl-coenzyme A
 Fatty tissues. See under Tissues
 Favism, glucose-6-phosphate dehydrogenase . . . 592
 F-distribution . . . 40, 41, 168, 169
 Fe. See Iron
 Feeces. See Faeces
 femto- (10⁻¹⁵) . . . 9
 Fennel, composition . . . 387 sq.
 Fermentation . . . 387, 390
 - alcoholic . . . 387, 390
 - lactic acid . . . 387 sq.
 Ferrium, properties and isotopes . . . 249
 Ferricytochromes . . . 359
 Ferriheme chloride . . . 359
 - hydroxide. See Haematin
 Ferri-hemochromogen . . . 359
 Ferrihemoglobin . . . 359
 - hydroxide . . . 359

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- L-fucose (*contd.*), in plasma 606
 - in plasma proteins 581
 - in saliva 645
 - in urine 673
 Fucosidolactose 324, 423
 Fumarase. See Fumarate hydratase
 Fumarate, in adenylic acid formation 436
 - from degradation of foodstuffs 402
 - in inosinic acid formation 435
 - in phenylalanine degradation 398
 - in tricarboxylic acid cycle 390, 391
 - in urea synthesis 443, 444
 Fumarate hydratase, in plasma 599
 - in tricarboxylic acid cycle 390, 391
 Fumarylacetoacetase in phenylalanine
 degradation 398
 Fumarylacetoacetic acid in phenylalanine
 degradation 398
 Functions, cyclometric 139
 - hyperbolic 140
 - trigonometric 138, 139
 Functional residual capacity (FRC) 541, 542, 550
 - in children nomograms 547
 fur (furlong) 200
 Furan 308
 Furan-2,5-dicarboxylic acid in urine 674
 Furanoses 308 sq.
 Furlong 200
- G**
- γ (gamma, microgramme) 204
 g (grade) 207
 g (gramme) 204, 213
 G ($giga$, 10^9) 9
 G . See D-Glucose
 G . See Guanosine
 Ga . See Gallium
 GABA. See γ -Amino- n -butyric acid
 Gadoleic acid 369
 Gadolinium, flame lines 284
 - properties, isotopes, etc. 240
 gal (gallon) 203
 Gal. See D-Galactose
 Gal (galileo) 210
 Galactocerebrosides 376
 Galactoflavin 472
 Galactokinase, in galactose diabetes 450
 - in lactic acid fermentation 390
 4'-(β -D-Galactopyranosido)-D-glucopyranose. See Lactose
 Galactosaemia 450
 D-Galactosamine (GalN) 314
 - in bile 655
 - in milk 689
 - 1-phosphate 319
 - in serum glycoproteins 606
 - in urine 673
 D-Galactose (Gal) 310, 314
 - in bile 655
 - in blood 450
 - in blood glycoproteins 606
 - in faeces 452
 - formation from glucose 420
 - glucose formation from 347
 - in lactic acid fermentation 390
 - in lipids 365
 - in urine 450, 673
 Galactose diabetes 450
 α -D-Galactose 1-phosphate 319
 - in erythrocytes 605
 - in lactic acid fermentation 390
 - in urine 450
 Galactose-1-phosphate uridylyltransferase in
 galactosaemia 450
 β -Galactosidase 412
 - in alactasia 451
 - in lactose intolerance 451
 - in seminal plasma 684
 Galactosyl- N -acetylgalactosaminyl-
 - in brain 377
 - in proplasts 375
 - in 323
 Galactosyl- N -acetylglucosaminyl-
 - in 311
 Galactosyl- N -acetylglucosaminyl-
 - in 210, 211
 Gallbladder, volume of contents 653
 Gallbladder bile. See Bile
 GALLI-MAININI test 715
 Gallium, flame lines 284
 - properties, isotopes, etc. 236
 Gallium-68, diagnostic use 289
 Gallon 204
 GalN. See D-Galactosamine
- Gametogenesis, gonadotropins in 714
 Gamma (unit) 204
 Gamma globulins. See γ -Globulins
 Gamma ray constant 221
 Gangliosides 365, 377
 - accumulation 455
 - brain, components 377
 - in brain and spinal cord 520
 - formation 424
 GAPDH. See Glyceraldehydephosphate
 dehydrogenase
 Garlic, composition 504
 Gases, blood. See under Blood
 - ideal, number density of molecules 228
 - molar volume 228
 - ionization 285, 286
 - standard temperature and pressure 541
 - volumes, reduction 259 sq.
 Gas-gangrene antitoxins, standards 760
 Gastric juice 647 sq.
 - acidity 648
 - effect of gastrin 739
 - amount 525, 647
 - electrolytes 525, 649
 - lipase 414, 650
 - proteolytic enzymes 407, 650
 - in stomach cancer. See Stomach cancer
 Gastric mucosa, enzyme activities 585
 Gastric ulcers, gastric acidity and 648
 Gastrin 407
 - in gastric juice 650
 Gastrin 739
 - effect on gastric juice acidity 648
 Gastritis, gastric juice albumin in 650
 Gastrointestinal tract, enzymes and
 precursors 406 sq.
 - effect of glucagon 738
 - hormones 739
 GAUCHER'S disease 377, 455
 - spleen cerebroside in 367
 Gauss 216
 Gb (gilbert) 216
 Ge groups of serum 634
 Gd. See Gadolinium
 GDH. See Glycero-phosphate dehydrogenase
 GDP. See Guanosine diphosphate
 Ge (germanium) 236
 Geiger counters 286
 Gelatin, amino acids 516
 - composition 513
 Gene mutations 446
 Genetic code 353
 Genistein, oestrogenic activity 755
 Genitals, surface area 528
 Genotypes, blood-group 626 sq.
 Gentamycin, reference preparation 762
 Geodetic units of length 200
 Geometric mean 137
 - series 136, 137
 Geometry 140 sq.
 Geranyl pyrophosphate in cholesterol
 synthesis 426, 427
 Germanium, properties, isotopes, etc. 236
 gf (gramme-force) 211
 GH-RF (growth-hormone releasing factor) 725
 gi (gill) 204
 GIERKE'S disease 450, 451
 giga- (10^9) 9
 Gigantism, pituitary, and ossification 707
 Gilbert 216
 GILBERT'S disease 454
 - serum bilirubin in 577
 Gill 204
 GI tract. See Gastrointestinal tract
 Gl (glucinium). See Beryllium
 Glands, composition 519
 Glauber's salt. See Sodium sulphate deca-
 hydrate
 Glc. See D-Glucose
 GlcN. See D-Glucosamine
 GLDH. See Glutamate dehydrogenase
 Gln. See Glutamine
 Globoside 377
 Globulin, BENCE-JONES, structure 581
 - in urine 668
 - thyroxine-binding 726
 Globulins 329
 - alpha-. See α -Globulins
 - beta-. See β -Globulins
 - gamma-. See γ -Globulins
 - myeloma, structure 581
 - osmotic activity 526
 - in pancreatic juice 652
 - in plasma and serum 582, 583
- α -Globulins, metabolism 579
 - in plasma and serum 582
 α_1 -Globulins in cerebrospinal fluid 637
 - in plasma and serum 582, 583
 - in semen 654
 - in synovial fluid 641
 - in urine 665
 α_2 -Globulins, allotypy 634
 - in cerebrospinal fluid 637
 - in plasma and serum 582, 583
 - in pregnancy and post partum 691
 - in semen 654
 - in synovial fluid 641
 - in urine 665
 β -Globulins, in cerebrospinal fluid 637
 - characteristics and function 550
 - metabolism 579
 - in plasma and serum 582, 583
 - in pregnancy and post partum 691
 - in synovial fluid 641
 - in urine 665
 β_{2M} -Globulin. See γ A-Globulin
 β_{2M} -Globulin. See γ M-Globulin
 γ -Globulins, allotypy 634
 - amino-acid composition 581
 - in blood 582, 583
 - in cerebrospinal fluid 637
 - characteristics and function 550
 - in gastric juice 656
 - in intestinal juice 656
 - metabolism 579
 - in pregnancy and post partum 691
 - structure 581
 - in synovial fluid 641
 - in rheumatoid arthritis 641
 - in urine 665
 γ_{12} -Globulin. See γ A-Globulin
 γ_{12} -Globulin. See γ M-Globulin
 γ_2 -Globulin. See γ G-Globulin
 γ_{2M} -Globulin. See γ G-Globulin
 γ A-Globulin, amino-acid composition 581
 - characteristics and function 550
 - in gastric juice 650
 - in milk 659
 - in saliva 645
 - in serum 580, 583
 - structure 581
 - in urine 665
 γ D-Globulin 550
 - structure 581
 γ E-Globulin 550
 - structure 581
 γ G-Globulin, amino-acid composition 581
 - in bile 655
 - characteristics and function 550
 - in faeces 659
 - in gastric juice 650
 - in semen 684
 - in serum 580, 583
 - structure 581
 - in urine 668
 γ M-Globulin, amino-acid composition 581
 - characteristics and function 550
 - in serum 580, 583
 - structure 581
 γ U-Globulin, structure 581
 Glomerular activity 531, 536
 - filtration rate 535
 - nephritis, fluid deprivation test in 733
 Glomerulotropin 531
 Glu. See L-Glutamate and L-Glutamic acid
 Glucagon 37, 738
 - in cyclic AMP formation 745
 - in catecholamine secretion 731
 α -Glucan-branching glycosyltransferase
 deficiency 450, 451
 α -1,4-Glucan-4-glucanohydrolase. See
 Amylase
 α -Glucan phosphorylase 451
 - deficiency 450, 451
 - in lactic acid fermentation 390
 - binding of pyridoxal phosphate 455
 - vitamin B₁₂ and 455
 Glucinium. See Beryllium
 D-Glucitol. See Sorbitol
 Glucocerebrosides, accumulation 377
 - in GAUCHER'S disease 379 sq., 748
 Glucocorticoids 379 sq., 748
 - determination 747
 - secretion, effect of ACTH 747
 Glucocorticosteroids. See Glucocorticoids
 α -D-Glucosyltransferase 451
 Glucosaminoglycans 747
 - action of corticosteroids 747

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- Gluconic acid 353
 β -phosphate 350
 D-Gluconic acid 310
 L-Gluconic acid 310
 D-Gluconic acid β -D-fructofuranose
 See Sucrose
 (L-D-Gluconic acid) β -D-glucopyranose See Maltose
 (L-D-Gluconic acid) β -D-glucopyranose 324
 Glucosamine (GlcN) 315
 in bile 355
 in cerebrospinal fluid 329
 formation 420, 423, 424
- Glucose
 in cerebrospinal fluid 329
 formation 420, 423, 424
- Glucose-6-phosphate isomerase, in gastric juice 650
 in glucose-6-phosphate formation from glyceraldehyde 3-phosphate 422
- Glucose-6-phosphate isomerase
 D-Glucose-6-phosphate NADP oxidoreductase See Glucose-6-phosphate dehydrogenase
 D-Glucose-6-phosphate phosphohydrolase See Glucose-6-phosphatase
 Glucose-1-phosphate wadyltransferase in carbohydrate synthesis and breakdown .. 441
 Glucose phosphatase See Phosphoglucomutase
- α -Glucosidase 412
 in α -glucosidase generalized glycosenosis 450, 451
 in intestinal mucosa 413
 in seminal plasma 684
 β -Glucosidase 412
 Glucosidase, in erythrocytes 449
 in fetal 452
 in ascorbic acid synthesis 489
 in blood 605
 in erythrocytes 605
 in feces 657
 formation from glucose 420, 423
 in gastric juice 650
 in urine 673
 β -Glucuronidase 412
 in blood 585, 597
 in pregnancy 585
 in gastric juice 650
 in seminal plasma 684
 in synovial fluid 641
 in urine 672
 in vaginal secretion 597
 β -Glucuronides 442
 β -D-Glucuronide glucuronohydrolase See β -Glucuronidase
 D-Glucuronolactone in ascorbic acid synthesis 489
 Glucuronic acid 642
 Glucuronic acid (GlcU) See Glutamine
 Glutamic acid (Glu) See L-lysine degradation
- Glutamine (Glu) 399
 in amino sugar formation 424
 in blood 574
 in blood protein 581
 cell constituents from 434
 in essential amino acid formation 438
 decarboxylation 374
 degradation 373, 374, 402
 in folate acid synthesis 478
 formation 420, 432
 glutathione from 438
 in guanidine acid formation 436
 in degradation of halogenobenzenes 445
 in histidine degradation 394, 395
 hydroxyproline from 432
 in isonic acid formation 433
 in milk 688
 in L-ornithine degradation 355
 in L-proline degradation 395
 proline from 432
 in saliva 645
 in sweat 680
 in transamination reactions 394
 with oxalacetate 420
 with pyruvate 420
 in urea synthesis 444
 in urine 667
- Glutamate dehydrogenase (GLDH), cell binding 585
 in glutamic acid degradation 393
 in isonic acid degradation 384
 in plasma 592
 in heart disease 587
 in liver disease 586, 587
 in tissues 585
- L-Glutamate NAD(P) oxidoreductase See Glutamate dehydrogenase
 Glutamate-oxaloacetate transaminase See Aspartate aminotransferase
 Glutamate-pyruvate transaminase See Alanine aminotransferase
- L-Glutamic acid (Glu) (see also L-Glutamate)
 Glutamic acid β -mononamide See Glutamine
 L-Glutamic γ -semialdehyde, in L-ornithine degradation 441
- formation 441
- in lactone acid fermentation 441
 in detoxication of halogenobenzenes 441
 in semen 441
 Glutathione reductase (GR), in plasma 441
 in seminal plasma 441
 in synovial fluid 441
 Gly See Glycine
 Glyceraldehyde, stereoisomerism 441
- glyceraldehyde
 in carbohydrate synthesis and breakdown 441
- in glycolysis 441
 in lactone acid fermentation 441
 in oxidation 441
 in pentose phosphate cycle 441
 Glyceraldehyde-3-phosphate dehydrogenase (GAPDH), in glycolysis 441
 in tissues 441
 D-Glyceraldehyde-3-phosphate ketolase See Triosephosphate isomerase
 D-Glyceraldehyde-3-phosphate NAD oxidoreductase See Glyceraldehyde-3-phosphate dehydrogenase
 D-Glycerate, in degradation of fats 441
 in acetic formation 441
 D-Glyceric acid (see also D-Glycerate)
 1,2-diphosphate See 1,2-Diphosphoglycerate
 2,3-diphosphate 441
 2-phosphate See 2-Phosphoglycerate
 3-phosphate See 3-Phosphoglycerate
 Glycine 1,2-cyclic phosphonic acid 441
 Glycines See Diglycerides, Mono-
 diglycerides, Diglycerides, Mono-
 diglycerols 441
 degradation 441
 in depot fat 39
 in lipids 441
 in plasma 441
 in urine 441
 Glyceral ester hydrolase See Lipase
 L-Glycerol 1-phosphate See L-Glycerol 1-phosphate
 L-Glycerol 3-phosphate NAD oxidoreductase See Glyceraldehyde-3-phosphate dehydrogenase
 Glyceral phosphocholine, enzymatic cleavage 441
 Glycerol trichloroacetic acid, formation 441
 α -Glycerophosphate (L-glycerol 1-phosphate) in degradation of fats 441
 formation from glucose 441
 in degradation of lecithin and cephalin 441
 Glycero-phosphate dehydrogenase (GDI) in glycerophosphate formation 441
 in plasma 441
 in tissues 441
 Glycero-phospholipids 441
 α -Glycerophosphonic acid (see also α -Glycophosphate) 441

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198.

[illegible]

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- β -Glycerophosphoric acid 375
 α -Glycerophosphorylcholine 376
 - in semen 683
 Glycerophosphorylcholine diesterase 417
 α -Glycerophosphorylcholine 376
 Glycine (Gly) 331
 - in bile 654 sq.
 - in blood 449, 574
 - buffers 280 sq.
 - cell constituents from 434
 - conjugation, with bile acids 438
 - in detoxication 444, 445
 - creatine from arginine, methionine and 437
 - degradation 397, 402
 - to oxalic acid 397, 449
 - in foods 516
 - formation 432
 - in glutathione formation 438
 - haem synthesis from 454
 - in inosinic acid formation 433
 - in milk 688
 - in porphyrin formation 437
 - in saliva 645
 - in serum proteins 581
 - in sweat 680
 - in L-threonine degradation 397
 - in transamination reactions 394
 - in urine 449, 667
 Glycinuria 452
 Glycoamine. See Guanidinoacetic acid
 Glycogen 327
 - in carbohydrate synthesis and breakdown 441
 - degradation 411
 - effect of catecholamines 733
 - effect of glucagon 738
 - deposition and utilization, inborn errors 450, 451
 - in erythrocytes 606
 - formation from glucose 420
 - in granulocytes 606
 - in lactic acid fermentation 390
 - in semen 684
 - in tissues 522
 Glycogenolysis. See Glycogen degradation
 Glycogenosis, idiopathic generalized 450, 451
 Glycogen phosphorylase. See α -Glucan phosphorylase
 Glycogen storage disease 415
 - erythrocyte glycogen in 606
 - glucagon in 738
 Glycogen synthetase. See UDPglucose-glycogen glucosyltransferase
 Glycoglycerides 365, 375
 Glycolaldehyde, active, in pentose phosphate cycle 421, 422
 Glycolaldehydetransferase. See Transketolase
 Glycol dehydrogenase, vitamin B₁₂ in 485
 Glycolic acid in urine 674
 Glycolipids 377
 N-Glycolylneuraminic acid 316
 Glycolysis 387 sq.
 Glycopeptides in urine 668
 Glycoproteins 327, 329
 - in bile 655
 - in blood 606
 - formation 347, 348, 350, 424
 - in urine 668
 α_1 -Glycoprotein, acid, characteristics and function 580
 - in bile 655
 - composition 581
 - in plasma 580
 - in saliva 645
 Glycosidases 309, 386, 405, 411 sq.
 Glycosides 308, 309
 Glycoside hydrolases 309, 386, 405, 411 sq.
 Glycosphingolipids 377
 Glycosuria. See Glucosuria
 Glycosyltransferases 386, 411 sq.
 Glycosyltransferase, α -glucan-branching, deficiency 450, 451
 Glycyl-glycine dipeptidase 408, 410
 Glycyl-leucine dipeptidase 410
 Glyoxalase in glycine degradation 397
 Glyoxalate. See Glyoxylate
 Glyoxylate, in glycine degradation 397
 - in L-hydroxyproline degradation 395
 - in plasma 607
 - in purine degradation 401
 - in transamination reactions 394
 Gm serum groups 634
 GMP. See Guanosine monophosphate
 Goat meat, composition 513
 Goat's milk, composition 511
 Goltre 727
 - cretinism and 449
 - diagnosis 289
 Gold, in blood 567
 - freezing point 209
 - properties, isotopes, etc. 242
 Gold-198, characteristics 293
 - decay table 305
 - gamma ray constant 221
 - therapeutic use 290
 Gold-199, characteristics 293
 'Golden section' 133
 Gonads, cholesterol synthesis 426
 - steroid hormones 428 sq.
 Gonadotropins, of anterior pituitary 713, 714
 - chorionic. See Chorionic gonadotropin
 - reference preparations 713, 763
 - releasing factors (GRF) 714
 - standards 763
 Gonadotropin-inhibiting factor in urine 714
 Gonane 381
 Gooseberries, composition 500
 Goose flesh, composition 513
 GOT (glutamate-oxalacetate transferase).
 See Aspartate aminotransferase
 Gout 453
 - serum uric acid 577
 - synovial fluid uric acid 641
 G-6-PDH. See Glucose-6-phosphate dehydrogenase
 GPT (glutamate-pyruvate transaminase). See Alanine aminotransferase
 gr (grain) 204
 GR. See Glutathione reductase
 Grade 138, 207, 208
 Grain 205
 Grain-force 211
 Gram. See Gramme
 Gramicidins, reference preparations 762
 Gramme 204
 - as energy unit 213
 Gramme-force 211
 Granuloblasts in bone marrow 621
 Granulocytes, blood count 618, 619
 - electrophoretic mobility 560
 - enzyme activities 585
 - glycogen 606
 - half-life 618
 Granulopoiesis in bone marrow 621
 Grapes, composition 500
 Grapefruit, composition 500
 Grape juice, composition 500
 Grape sugar. See D-Glucose
 GRAVES' disease 718
 Gravitational constant 201, 228
 Gravity, acceleration due to 211, 230
 Greek alphabet 9
 Gregorian year 206
 grf (grain-force) 211
 GRF (gonadotropin-releasing factors) 714
 GRF (growth-hormone releasing factor) 725
 GROTHUS-DRAPER law 218
 Growth, body composition and 517
 - growth hormone and 720
 - intrauterine 691, 692
 - normal measurements during 693 sq.
 - thyroxine deficiency and 727
 Growth hormone 719, 720
 - releasing factor (GRF) 725
 - standard and reference preparation 762
 Gs (gauss) 216
 GSH. See Glutathione
 GSSG. See Glutathione
 GTP. See Guanosine triphosphate
 Guanase. See Guanine deaminase
 Guanidine, in blood 573
 - in urine 666
 Guanidinoacetic acid 335
 - in blood 573
 - in creatine formation 437
 - in urine 666
 Guanine 338
 - enzymatic deamination 419
 - degradation 401
 - in DNA synthesis 352
 - in protein synthesis 353
 - in purine degradation 400
 - in RNA synthesis 352
 - in urine 671
 Guanine aminohydrolase. See Guanine deaminase
 Guanine deaminase 401, 419
 - in plasma 598
 - in purine degradation 400
 Guanosine (G, Guo) 339
 - in purine degradation 400
 Guanosine deaminase 401
 - in purine degradation 400
 Guanosine diphosphate (GDP) 343
 Guanosine diphosphate cobinamide in vitamin B₁₂ synthesis 484
 Guanosine diphosphate L-fucose 347
 - in L-fucose formation 423
 - milk oligosaccharides from 423
 Guanosine diphosphate 4-keto-6-deoxy-L-galactose in L-fucose formation 423
 Guanosine diphosphate 4-keto-6-deoxy-D-mannose in L-fucose formation 423
 Guanosine diphosphate mannose 347
 - in L-fucose formation 423
 Guanosine monophosphate (GMP) 343
 - formation 436
 - in purine degradation 400, 401
 - in RNA 351
 Guanosine triphosphate (GTP) 343
 - in adenylic acid formation 435
 - in ATP synthesis 404
 - in blood 577
 - in protein synthesis 354
 - in tricarboxylic acid cycle 391
 - in vitamin B₁₂ synthesis 484
 Guanylate deaminase 401
 - in purine degradation 400
 Guanylic acid. See Guanosine monophosphate
 D-Guloheptulose 311
 L-Gulonolactone in ascorbic acid synthesis 489
 L-Gulonolactone oxidase in ascorbic acid synthesis 489
 D-Gulose 310
 GÜNTHER'S disease 454
 Guo. See Guanosine
 H 9
 h (hecto, 10²) 205
 h (hour) 216
 H (henry) 216
 H. See Hydrogen
 ha (hectare) 203
 Haddock, composition 514
 Haem 359 sq.
 - derivatives 359 sq.
 - proteins 329, 360 sq.
 - synthesis 454
 Haematin 359, 360, 362
 - in faeces 657
 Haematocrit (Ht) 613, 614, 617
 - blood acid-base balance and 557
 - blood viscosity and 554
 - body 691
 - gain in pregnancy 615
 - mean corpuscular volume from 531
 - renal blood flow and 691
 - venous, gain in pregnancy 677
 Haematoidin in urinary sediments 359
 Haematoporphyrin 763
 Haemoglobin. See Methaemoglobin
 Haemoglobinocyanide reference preparation 359
 Haemin 359
 Haemoblastosis, serum adenosine deaminase 362
 Haemochromes 359
 Haemochromogen 531 sq.
 Haemodynamics, renal 359, 360, 362
 Haemoglobin (Hb) 359, 360, 362
 - in whole blood 576, 579, 615, 617
 - and haematocrit 614, 615
 - gain in pregnancy 691
 - and pH of body fluids 527
 - breakdown 362
 - cyanide, haemoglobin determination as 615
 - embryonic 576
 - in erythrocytes 615
 - foetal 448
 - persistence 576
 - haptoglobin binding 506
 - iron content 615, 617
 - mean corpuscular 614, 615
 - and haematocrit 570
 - oxygen binding 578
 - in plasma 446 sq.
 - types 661, 671
 - in urine 446 sq.
 Haemoglobinopathies 621
 Haemogram, SCHILLING'S 614
 Haemolysis, erythrocyte thickness and 573
 - glutathione stability and 573

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- 1-Hydrogen-1 atom, Bohr radius 228
 - mass 229
 - RYDBERG constant and frequency 229
 1-Hydrogen-3, characteristics 234, 292
 Hydrogen electrode, redox potential 403
 1-Hydrogen-ion concentration, definition 278
 1-Hydrogen peroxide in glycine degradation 397
 Hydrolases 386
 1-Hydro-lyases 386
 Hydrosphere, composition 234 sq.
 1-Hydroxamic acids from fatty acids 414
 1-Hydroxocobalamin 482, 483
 3-Hydroxyacyl-CoA dehydrogenase in degradation of fats 392
 β -Hydroxyacyl-coenzyme A in degradation of fats 392
 11-Hydroxyandrost-4-en-17-one in urine .. 746, 749
 3 α -Hydroxy-5 α -androst-17-one. See Androst-17-one
 3 α -Hydroxy-5 β -androst-17-one. See Androst-17-one
 3 β -Hydroxy-5 α -androst-17-one. See Androst-17-one
 3 β -Hydroxy-5 β -androst-17-one. See Androst-17-one
 3 β -Actiocholanolone
 11 β -Hydroxy- Δ^4 -androstene-3,17-dione, biosynthesis 428, 429
 - breakdown 746
 19-Hydroxy- Δ^4 -androstene-3,17-dione, biosynthesis 428, 429
 - in oestrogen synthesis 431
 3 β -Hydroxyandrost-5-en-17-one. See Androst-17-one
 17 α -Hydroxyandrost-4-en-3-one 380
 17 β -Hydroxyandrost-4-en-3-one. See Androst-17-one
 11-Hydroxyandrost-4-en-3-one 746, 749
 3-Hydroxyanthranilic acid, in tryptophan metabolism 398, 399, 475
 - in urine 668
 5-Hydroxybenzimidazolecyanocobamide 483
m-Hydroxybenzoic acid in urine 675
 β -Hydroxybutyrate, in blood 608
 - in cerebrospinal fluid 639
 - conversion factor into acetone 251
 - in degradation of fats 393
 - in urine 674
 α -Hydroxybutyrate dehydrogenase (HBDH), in plasma 591
 - in pregnancy 586
 3-Hydroxybutyrate dehydrogenase in degradation of fats 393
 β -Hydroxy- γ -butyrobetaine. See Carnitine
 3-Hydroxy- β -carotene 458
 25-Hydroxycholecalciferol 461, 809
 Hydroxycorticosteroids. See under Corticosteroids
 17 α -Hydroxycorticosterone. See Cortisol
 18-Hydroxycorticosterone, secretion rates 743
 2 α -Hydroxycortisol 428
 6 β -Hydroxycortisol, breakdown 746
 - in urine 747
 16-Hydroxydehydroepiandrosterone in urine 746, 747
 17 α -Hydroxydeoxycorticosterone, biosynthesis 428, 429
 18-Hydroxydeoxycorticosterone, biosynthesis 428, 429
 4-Hydroxydihydropteridine in phenylalanine-tyrosine conversion 439
 25-Hydroxyergocalciferol 809
 Hydroxyestr-1. See Hydroxyestr-1
 α -Hydroxyethyl-2-thiamine diphosphate 469
 β -Hydroxyethyltrimethylammonium hydroxide. See Choline
 γ -Hydroxyglutamic acid in L-hydroxyproline degradation 395
 α -Hydroxyglutaric acid in glycine degradation 397
 γ -Hydroxyglutaric acid in L-hydroxyproline degradation 395
 2-Hydroxyhexadecanoic acid 372
m-Hydroxyhippuric acid in urine 666
 5-Hydroxyindoleacetaldehyde from 5-hydroxytryptamine 441
 5-Hydroxyindoleacetic acid, from 5-hydroxytryptamine 441
 - in urine 669
 Hydroxyindole O-methyltransferase in melanin formation 730
 β -Hydroxyisobutyric acid in valine degradation 396
 β -Hydroxyisobutyryl-coenzyme A in valine degradation 396
 8-Hydroxykynurenic acid in tryptophan degradation 398, 399
 3-Hydroxykynurenine, in tryptophan degradation 398, 399, 475
 - in urine 669
 1-Hydroxylases 385
 8-Hydroxyllysine 331
 6-Hydroxymelatonin 730
 Hydroxymethyltyrosidic acid synthesis 479
 1-Hydroxymethylglutaryl-coenzyme A, in cholesterol synthesis 426, 427
 - in leucine degradation 395
 Hydroxymethyltetrahydrofolic acid, in glycine degradation 397
 - in glycine formation 432
 - in transfer of one-carbon groups 436, 437
 1-Hydroxymethyltransferases 385
 α -Hydroxymuconic semialdehyde in tryptophan degradation 399
 α -Hydroxymyristic acid 372
 1-Hydroxynervonic acid 372, 377
 2-Hydroxyoctadecanoic acid 372
iii-12-Hydroxy- Δ^8 -octadecenoic acid 372
 15 β -Hydroxyoestradiol-17 β in urine 756
 3-Hydroxyoestra-1,3,5(10),6,8-penten-17-one. See Equilenin
 3-Hydroxyoestra-1,3,5(10),7-tetraen-17-one 380
 3-Hydroxyoestra-1,3,5(10)-trien-17-one. See Oestrone
 2-Hydroxyoestrone, biosynthesis and metabolism 431
 6 α -Hydroxyoestrone, biosynthesis and metabolism 431
 6 β -Hydroxyoestrone, biosynthesis and metabolism 431
 11 β -Hydroxyoestrone from oestrone 431
 15 α -Hydroxyoestrone in urine 756
 15 β -Hydroxyoestrone in urine 756
 16 α -Hydroxyoestrone, biosynthesis and metabolism 431
 - in urine 756
 - in pregnancy 757
 16 β -Hydroxyoestrone, biosynthesis and metabolism 431
 - in urine 756
 18-Hydroxyoestrone, biosynthesis and metabolism 431
 - in pregnancy urine 432
 α -Hydroxypalmitic acid 372
 p -Hydroxyphenylacetic acid in urine 675
 p -Hydroxyphenylpyruvic acid in phenylalanine degradation 398
 3 α -Hydroxy-5 α -pregnan-20-one 379
 3 α -Hydroxy-5 β -pregnan-20-one. See Pregnanolone
 17 α -Hydroxypregn-4-ene-3,20-dione. See 17 α -Hydroxypregsterone
 21-Hydroxypregn-4-ene-3,20-dione. See 11-Deoxycorticosterone
 21-Hydroxypregn-4-ene-3,11,20-trione. See Dehydrocorticosterone
 16-Hydroxypregnenolone in urine 747
 21-Hydroxypregnenolone. See 11-Deoxycorticosterone
 3 β -Hydroxypregn-5-en-20-one. See Pregnanolone
 20-Hydroxypregnenones 380, 753
 - in plasma 754
 17 α -Hydroxypregsterone 380, 753
 - biosynthesis 428, 429
 - breakdown 746
 - in plasma 754
 20-Hydroxypregsterones. See 20-Hydroxypregnenones
 Hydroxyprolinaemia 449
 L-Hydroxyproline (Hyp) 331
 - in blood 449, 574
 - degradation 394, 395, 402
 - formation 432
 - ascorbic acid in 490
 - in proteins 420
 - in urine 449, 666, 667
 - parathyroid hormone and 728
 6-Hydroxypurine. See Hypoxanthine
 γ -Hydroxypyrrolidine- α -carboxylic acid. See Hydroxyproline
 3-Hydroxypyrrolidine-5-carboxylate reductase in hydroxyprolinaemia 449
 Hydroxypyruvate, in serine formation 432
 - in transamination reactions 394
 α -Hydroxystearic acid 372
 Δ^3 - β -Hydroxysteroids, structure and assay 744
 21-Hydroxysteroids, deficient synthesis 456
 3 β -Hydroxysteroid dehydrogenase deficiency 456
 2-Hydroxytetraacosanoic acid. See Cerebronic acid
 2-Hydroxy- Δ^{14} -tetraacosenoic acid 372, 377
 2-Hydroxytetradecanoic acid 372
 18-Hydroxytetrahydrocorticosterone in urine 430
 4-Hydroxytetrahydropteridine in phenylalanine-tyrosine conversion 439
 2-Hydroxytricosanoic acid 372
 5-Hydroxytryptamine. See Serotonin
 5-Hydroxytryptophan, decarboxylation 394
 - formation, dehydroascorbic acid and 490
 - in 5-hydroxytryptamine formation 441
 - in tryptophan metabolism 475
 3-Hydroxytyramine. See 3,4-Dihydroxyphenylethylamine
 β -Hydroxyvaleryl-coenzyme A in norleucine degradation 396
 Hygromycin B, standard 762
 Hyl (8-hydroxyllysine) 331
 Hyp. See L-Hydroxyproline
 Hypoadrenalism, aldosterone secretion 745
 - sweat sodium and chloride in 680
 Hyperaemia 450
 Hyperbilirubinaemia 454, 455
 - posthepatic, serum bilirubin 577
 Hyperbolic functions 140
 Hypercalcaemia, idiopathic, of infancy 464
 Hypercalcaemia 453
 Hypercalcaemia 453
 Hypercholesterolaemia 456
 Hyperchromia 615
 Hypergeometric distribution 77, 109 sq., 189 sq.
 Hyperglobulinaemia, serum viscosity 558
 Hyperglycaemia 449
 Hyperkeratosis, follicular 460
 Hyperlipaemia 374
 - essential familial 456
 Hyperparathyroidism 728
 Hyperprolinaemia 449
 Hypersomatotropism 719
 Hypertension 740, 741
 - essential, fluid deprivation test 535
 - urinary concentration 533
 Hyperthyroidism 287, 288, 727
 - radiotherapy 291
 - serum protein-bound iodine 564
 Hyperuricaemia. See Gout
 Hyperventilation, effect on blood acid-base balance 569
 Hypochromia 615
 Hypo- γ -globulinaemia 449
 Hypoglycaemia, leucine-sensitive 451
 Hypophosphataemia 452
 Hypophosphatosis 415
 Hypoparathyroidism 449
 Hypoproteinaemia 467, 468
 - vitamin K and 467
 Hypotaurine in taurine formation 438
 Hypothalamus, regulation of ACTH secretion by 717
 - effect on growth hormone secretion 720, 723
 - oxytocin and vasopressin formation 722, 723
 - pituitary-regulating factors 725
 - effect on prolactin secretion 718, 719
 - releasing and inhibiting factors 725, 820
 Hypothyroidism 287, 288, 727
 - and ossification 707
 - serum protein-bound iodine 564
 Hypoventilation, effect on blood acid-base balance 569
 Hypoxanthine 338
 - enzymatic oxidation 410
 - in plasma 577
 - in purine degradation 460, 461
 - in urine 671
 Hypoxanthine oxidase. See Xanthine oxidase
 Hz (hertz, cycle per second) 214
 I. See Inosine
 I. See Iodine
 IC (inspiratory capacity) 542, 551
 ICAO standard atmosphere 252 sq.
 ICDH. See Isocitrate dehydrogenase
 ICSH (interstitial cell-stimulating hormone). See Luteinizing hormone
 Icteric hepatitis, bile composition 635
 Ideal gases. See under Gases
 - solutions 270

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198.

[illegible]

- Involution 132
- Iodide. See Iodine
- Iodine, absorption and utilization 440
- atomic weight multiples 250
 - in cerebrospinal fluid 636
 - dietary requirements 494, 497
 - in faeces 658
 - in milk 688
 - in plasma 564, 726
 - butanol-extractable 564
 - protein-bound 564
 - properties, isotopes, etc. 239
 - renal clearance 726
 - in saliva 644
 - decinormal solutions 277
 - in sweat 679
 - in thyroid gland 725
 - in thyroid hormone formation 440
 - uptake by organs 726
 - in urine 663
- Iodine-125, characteristics 293
- decay table 303
 - diagnostic use 289
- Iodine-130, characteristics 293
- gamma ray constant 221
- Iodine-131, specific activity 217
- characteristics 293
 - decay table 303
 - diagnostic use 287 sq.
 - gamma ray constant 221
 - in thyroid function tests 287 sq.
 - in thyroid scintigraphy 288, 289
- Iodine-132, characteristics 293
- decay table 304
- Iodinium ions in thyroid hormone formation 440
- L-Iodogorgoleic acid. See L-3,5-Di-iodotyrosine
- o-Iodohippuric acid in kidney radiography 289
- Iodopsin 457
- Ion, definition 270
- Ion dose from radionuclides 219
- Ionic concentration 227
- Ionium (^{238}Th), properties 246
- Ionization of gases 285, 286
- IPTS-68 (International Practical Temperature Scale) 209
- Ir. See Iridium
- Iridium, properties, isotopes, etc. 242
- Iridium-192, characteristics 293
- decay table 305
 - gamma ray constant 221
 - therapeutic use 290
- Iron, atomic weight multiples 250
- in bile 654
 - in blood 566
 - in whole body 517
 - in bones and teeth 521
 - in cerebrospinal fluid 636
 - dietary requirements 494, 496
 - in faeces 658
 - flame lines 284
 - in foods 499 sq.
 - in hair and nails 520
 - metabolism, tracer study 289
 - in milk 688
 - in organs 519
 - properties, isotopes, etc. 236
 - in skin 520
 - in sweat 680
 - in synovial fluid 641
 - in urine 664
- Iron-54, gamma ray constant 221
- Iron-55, characteristics 292
- Iron-59, characteristics 292
- decay table 296, 297
 - diagnostic use 289
- Iron porphyrins 359 sq.
- in biological oxidations 402, 403
 - degradation 401
- Irradiance 222
- Irrational numbers 132
- IRV (inspiratory reserve volume) 541
- Isoalloxazine 336
- Isoandrosterone. See Epiandrosterone
- Isobutyric acid 371
- Isobutyryl-coenzyme A in valine degradation 396
- Isocaproic acid, in synthesis of adrenal steroids and androgens 428, 429
- in cholesterol breakdown 401
 - degradation 401
- Isocitrate in tricarboxylic acid cycle 390, 391
- Isocitrate dehydrogenase (ICDH), cell binding 585
- in cerebrospinal fluid 638
 - in gastric juice 650
- Isocitrate dehydrogenase (ICDH), isozymes 584
- in plasma 591
 - in pregnancy 586
 - in seminal plasma 684
 - in synovial fluid 641
 - in tissues 585
 - in tricarboxylic acid cycle 390, 391
- threo-D₂-Isocitrate:NADP oxidoreductase. See Isocitrate dehydrogenase
- Iso-(β)-crotonic acid 368
- Isodulcitol 313
- Isoenzymes. See Isozymes
- L-Isoleucine (Ile) 332
- in blood 449, 574
 - in blood proteins 581
 - in cerebrospinal fluid 449
 - degradation 395, 396, 402
 - dietary requirements 496
 - in foods 516
 - in milk 688
 - in saliva 645
 - in urine 667
- Iso maltase. See Oligo-1,6-glucosidase 451
- Iso maltose, hydrolysis 412
- Iso merases 386
- in vitamin A metabolism 457
- cis-trans-Isomerases. See Cis-trans isomerases
- Isomeric nuclides 217
- cis-trans Isomerism. See Cis-trans isomerism
- Iso myristic acid 371
- Isopentenyl pyrophosphate, in cholesterol synthesis 426, 427
- in vitamin A synthesis 457
- Iso sthenuria 534
- Isotocin 724
- Isotonic solutions 526
- calculation 271
- Isotopes. See Nuclides and Radionuclides
- Isovaleric acid 371
- Isovaleryl-coenzyme A in leucine degradation 395
- Isozymes 584
- tissue-specific, in diagnosis 586
- ITP. See Inosine triphosphate
- J**
- J (joule) 212, 213, 216
- JAFFÉ reaction 572
- Jaundice (see also Kernicterus) 362, 576, 577
- haemolytic, erythrocyte osmotic resistance 616
 - of newborn 577
 - idiopathic, chronic 454
 - nonhaemolytic, congenital 454
 - obstructive, serum enzyme changes 587
 - serum glucosephosphate isomerase 600
 - serum ketose-1-phosphate aldolase 599
 - serum 5'-nucleotidase 597
 - simple, of infants 576, 577
- JENSEN's sarcoma, lactic acid fermentation 388
- respiratory rate 387
- Joule 212, 213, 216, 222
- Julian year 206
- K**
- k (kilo-, 10^3) 9
- K (kelvin) 208, 209, 213
- K. See Potassium
- Kale, composition 504
- Kallidins 742
- Kallikrein 742
- Kallikreinogen 742
- Kanamycins, reference preparations 761
- KARLEN-WROBLEWSKI enzyme units 584
- Kell blood-group system 631
- clinical significance 633
- Kelvin 208, 209
- as energy unit 213
- KELVIN temperature scale 208, 209
- Keratin 377
- lignoceric acid in 367
- Keratan sulphate 328
- Keratosulphate 328
- Kernicterus 362, 454, 577
- glucose-6-phosphate dehydrogenase 592
- Ketals 308
- Ketachup, composition 506
- degradation 449
- Keto acids in urine 449
- 3-Ketoacid-CoA transferase in degradation of fats 393
- Keto acid-lyases 386
- 3-Ketoacyl-CoA thiolase in degradation of fats 392
- β -Ketoacyl-coenzyme A in degradation of fats 392
- α -Ketoadipic acid, in L-lysine degradation 398
- in tryptophan degradation 399
- 11-Ketoetiocholanolone in urine 746, 749
- α -Keto- ϵ -aminocaproic acid in L-lysine degradation 398
- α -Keto- δ -aminovaleric acid in D-orithine and D-proline degradation 395
- γ -Keto- δ -aminovaleric acid. See δ -Amino-laevalinic acid
- 11-Ketoandrosterone in urine 746
- 2-Keto-D-arabohexose. See D-Fructose
- α -Ketobutyric acid, in homoserine degradation 397
- in L-threonine degradation 397
- α -Ketocaproic acid in norleucine degradation 396
- 16-Ketoestradiol. See 16-Keto-estradiol
- 17-Ketogenic steroids. See under Corticosteroids
- α -Ketoglutarate, reductive amination 432
- in ATP synthesis 404
 - in blood 607
 - in cerebrospinal fluid 639
 - in cysteinylsulphonic acid formation 438
 - from degradation of foods 402
 - in glutamic acid degradation 393, 394
 - in glutamic acid formation 432
 - in glycine degradation 397
 - in L-hydroxyproline degradation 395
 - in L-orithine degradation 395
 - in transamination reactions 394, 395
 - in tricarboxylic acid cycle 390, 391
 - in urea synthesis 444
 - in urine 674
- α -Ketoglutaric semialdehyde in glycine degradation 397
- α -Keto- γ -guanidinovaleric acid in transamination reactions 394
- 2-Keto-L-gulonate 489
- in ascorbic acid synthesis 489
- Ketohexokinase, in fructosuria 430
- in lactic acid fermentation 594
 - in plasma 608
- α -Ketoisocaproic acid, in blood 395
- in leucine degradation 449
 - in maple syrup urine disease 607
- α -Ketoisovaleric acid, in blood 449
- in maple syrup urine disease 487
 - pantothenic acid from 396
 - in valine degradation 608
- α -Keto- β -methylvaleric acid, in blood 396
- in isoleucine degradation 449
 - in maple syrup urine disease 461, 463
- Ketone 250 461, 463
- Ketone bodies, conversion factors into acetone 251
- in blood 608
 - accumulation in tissues 393
 - in urine 674
- α -Ketonic acids in amino-acid degradation 393, 394
- 16-Keto-estradiol, biosynthesis and metabolism 431
- in urine 755
 - in pregnancy 757
- 6-Keto-oestrone, biosynthesis and metabolism 431
- 11-Keto-oestrone, biosynthesis and metabolism 431
- 16-Keto-oestrone, biosynthesis and metabolism 431
- α -Ketopantoic acid in pantothenic acid synthesis 467
- Ketopentoses in urine 673
- 3-Keto-6-phosphogluconic acid in pentose phosphate cycle 421, 422
- Ketoses 368 sq.
- Ketose-1-phosphate aldehyde-lyase. See Ketose-1-phosphate aldolase
- Ketose-1-phosphate aldolase, in lactic acid fermentation 599
- in plasma 587
 - in heart disease 587
 - in hepatic coma 586
 - in tissues 393
- Ketosis 744
- in plasma 745
- Δ^4 -3-Ketosteroids, assay and structure 744
- 17-Ketosteroids, assay and structure 746 sq.
- in urine 456
 - diminished 456

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198.

[illegible]

- Levo compounds 308, 309
 Levulose. See D-Fructose
 Lewis blood-group system 631, 632
 - clinical significance 633
 Lymph cells, seminal fructose and 684
 L.H. See Luteinizing hormone
 L.H.-RF. See Luteinizing-hormone releasing factor
 Li (link) 200
 Li. See Lithium
 Life expectation, blood pressure and 553
 - body weight and 712
 Ligases 386
 Light, quantities and units 222 sq.
 - velocity 215, 216, 228
 Light year 201
 Lignoceric acid 367
 - in keratin 377
 Lime juice, composition 500
 Limit-dextrins. See Dextrins
 Lincomycin, reference preparation 762
 Linderic acid 368
 Line (unit) 200
 Linear equations, solution 137
 Linear velocity units 210
 Link 200
 Linoleic acid 370, 492
 - in bile 655
 - in depot fat 374
 - dietary requirements 492, 495
 - in foods 498 sq.
 - in serum lipids 604
 - in milk 687
 Linoleyl alcohol 492
 Lipases 405, 414
 - in bile 655
 - in cerebrospinal fluid 638
 - in gastric juice 650
 - in milk 689
 - in pancreatic juice 652, 653
 - in plasma 595
 - in pancreatic disease 587
 Lipids (*see also Fats*) 365 sq.
 - in bile 655
 - biosynthesis, inhibition by nicotinic acid 477, 478
 - in blood 600 sq.
 - excess 374, 456
 - in brain and spinal cord 520
 - in cerebrospinal fluid 638
 - 'compound' 365
 - in erythrocytes 600, 601
 - in faeces 659, 660
 - in gastric juice 650
 - in intestinal juice 656
 - in leucocytes 601
 - metabolism, effect of ACTH 717
 - effect of corticosteroids 749, 750
 - disturbance 455
 - effect of glucagon 738
 - effect of growth hormone 720
 - in pancreatic juice 652
 - in semen 685
 - 'simple' 365
 - in sweat 681
 - in synovial fluid 642
 - in thrombocytes 601
 - in urine 675
 Lipid phosphorus, in blood 563
 - conversion factors to phosphorus 251
 - in erythrocytes 563
 - in milk 689
 - in semen 683
 Lipidoses 455, 456
 α -Lipoic acid 492
 - in plasma 608
 - in oxidation of sugars 391
 - in tricarboxylic acid cycle 390, 391
 Lipoid factor in blood coagulation 622
 Lipoproteins 329
 - accumulation 456
 - allotypy 634
 - and cholesterol 374
 - in serum 602
 - in spermatozoa 685
 α -Lipoproteins in serum 580, 602
 α_1 -Lipoprotein, characteristics and function 580
 - in erythrocyte sedimentation 559
 - in serum 580, 583
 α_2 -Lipoprotein, characteristics and function 580
 - in serum 580
 β -Lipoproteins, in cerebrospinal fluid 637
 - in serum 602
 β_1 -Lipoprotein, characteristics and function 580
 β_2 -Lipoprotein in serum 580, 583
 Lipotropic hormone (LPH) 716
 Lipotropin 716
 liq.pt (liquid pint) 204
 liq.qt (liquid quart) 204
 Liquid measures 204
 Liter. See Litre
 Lithium, flame lines 284
 - in plasma 567
 - properties, isotopes, etc. 234
 Lithocholic acid, in bile 655
 - in faeces 660
 Lithosphere, composition 234 sq.
 Litmus indicator 283
 Litre 203
 Litre atmosphere 213
 Liver, adipohepatic, serum enzyme changes 586
 - animal, amino acids 516
 - composition 512 sq.
 - ascorbic acid 490
 - biotin 486
 - contribution to BMR 539
 - carcinoma, serum enzyme changes 587
 - serum triosephosphate isomerase 600
 - carnitine 491
 - cholesterol synthesis 426
 - cirrhosis 451, 455, 456
 - bile acids 655
 - biliary bilirubin 654
 - gastric juice ammonia 649
 - gastric juice secretion 647
 - leucocyte zinc 567
 - serum, bilirubin 577
 - enzyme changes 586
 - pantothenic acid 611
 - composition 519
 - deaminases 419
 - disease, glucuronic acid excretion 673
 - serum, adenosine deaminase 599
 - arginase 598
 - cholinesterase 595
 - dehydrogenases 590 sq.
 - enzyme changes 586
 - glucose-6-phosphatase 597
 - glucosephosphate isomerase 600
 - β -glucuronidase 597
 - guanine deaminase 598
 - ketose-1-phosphate aldolase 599
 - alkaline phosphatase 596
 - phosphopyruvate hydratase 600
 - ribosephosphate isomerase 600
 - transaminases and transferases 593, 594
 - dysfunction 454
 - enlargement 449, 451 sq.
 - enzyme activities 585
 - enzyme activity gradients between serum and 586
 - fatty acid esterases 414
 - glycogen accumulation 451
 - glycosidases 411 sq.
 - effect of insulin 736, 737
 - lactic acid fermentation 388
 - lipid accumulation 455
 - S-methyltetrahydropteroylglutamic acid 479
 - nicotinic acid 477
 - oxidases 419
 - pantothenic acid 488
 - peptidases 410
 - phosphatases 415, 416
 - phospholipases 417
 - porphyrins 454, 455
 - purine nucleoside phosphorylase 418
 - radiography 289
 - respiratory rate 387
 - riboflavin 471
 - thiamine 470
 - thyroid hormones 727
 - transaminations 394
 - vitamin A 457
 - vitamin B₆ 475
 - vitamin B₁₂ 484
 - weight 710
 Liver starch. See Glycogen
 lm (lumen) 222
 LMTH (luteomammotropic hormone). See Prolactin
 In. See Logarithms
 Lobster, composition 515
 log. See Logarithms
 log₁₀ e 9
 log₁₀ 10 9
 Loganberries, composition 500
 Logarithms, common 10
 - of factorials 26, 27
 Logarithms, explanation 134, 135
 - natural 12 sq.
 Logistic weights 57
 Logits and antilogits 56
 Long-acting thyroid stimulator (LATS) 718
 Long ton 205
 Loschmidt constant 228
 Loudness quantities and units 225, 226
 Lp groups of serum 634
 LPH (lipotropic hormone) 716
 Lr (lawrencium) 243
 LRF. See Luteinizing-hormone releasing factor
 LSI (leucocyte sedimentation index) 558
 LTH (luteotropic hormone). See Prolactin
 Lu (lutetium) 241
 Lumbar fluid. See Cerebrospinal fluid
 Lumen 222
 Lumiflavin 472
 Luminous quantities and units 222 sq.
 Lumisterol in vitamin D₂ formation 461, 463
 Lungs, blood pressure 553
 - capacity values 541 sq., 550, 551
 - in children, nomograms 547
 - circulation 543, 544
 - compliance. See Compliance
 - composition 512, 519
 - diffusing capacity 545, 552
 - enzyme activities 585
 - lactic acid fermentation 388
 - peptidases 410
 - resistance. See Pulmonary resistance
 - values 541 sq.
 - calculation from spirometer values 239 sq.
 - ratios 551
 - vital capacity. See Vital capacity
 - volumes 541, 542
 - water loss from 524
 - weight 710
 - xanthine oxidase 419
 Luteinizing hormone (LH) 713, 714
 - oestrogens and 757
 - progesterone secretion and 754, 755
 - secretion, effect of testosterone 753
 Luteinizing-hormone releasing factor (LRF, LH-RF) 714, 725
 - effect of testosterone 753
 Luteomammotropic hormone. See Prolactin
 Luteotropic hormone. See Prolactin
 Lutetium, properties, isotopes, etc. 241
 Lutheran blood-group system 633
 - clinical significance 633
 Lux (lux) 223
 lx (lux) 201
 l.y. (light year) 201
 Lyases 365
 Lymecycline, reference preparation 762
 Lymphadenosis, leucocyte mobility 563
 Lymphatic tissues, action of corticosteroids 750
 Lymph glands, enzyme activities 585
 Lymphocytes, blood count 618 sq.
 - in bone marrow 621
 - dimensions 618
 - electrophoretic mobility 560
 - histamine 575
 - in synovial fluid 640
 Lymphocyte-stimulating factor 730
 Lymphosarcoma, serum ribosephosphate isomerase 610
 Lys. See L-Lysine
 L-Lysine (Lys) 332
 - in blood 574
 - in blood proteins 581
 - decarboxylation 394
 - degradation 378, 402
 - dietary requirements 496
 - in foods 516
 - formation from α , ϵ -diaminopimelic acid 394
 - in milk 645
 - in saliva 645
 - in sweat 663
 - in urine 452, 667
 Lysine vasopressin. See Vasopressin
 Lysokinases 622
 Lysolecithins, in bile 635
 - in cerebrospinal fluid 637
 - enzymatic cleavage 604
 - in erythrocytes 540
 - in erythrocyte sedimentation 375, 376
 - formation 614
 - in plasma 417
 Lysoleipids from phospholipids 417
 Lysophosphatides 365, 375, 376

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198.

isophosphase	417
me	413
nine juice	650
"	289
ose	310
ucose. See D-Xylose	
alose See L-Xylose	
cro-, 10 ⁻⁶)	9
cron, micrometre)	200
(re).	200
(ill-, 10 ⁻³)	9
ega-, 10 ³)	9
(e unit	217
hydratase	
L-Maleate NAD(P) oxidoreductase. See	
Maleate dehydrogenase	
Malylacetacetic acid in phenylalanine	
diaminon	208
- in saliva	646
- from starch	411
Mammary glands, effect of oxytocin . .	723
- phosphatases	415
- effect of prolactin	719
- weight gain in pregnancy	690
Mammotropin. See Prolactin	
Man. See D-Mannose	
Manganese, atomic weight multiples . .	259
- in bile	654
- in blood	567
- in cerebrospinal fluid	636
- dietary requirements	497
- in feces	658
- flame lines	284
- in foods	499 sq.
- activation of histone dephosphatase .	415
- in milk	688
- in organs	519
- properties, isotopes, etc	234
- activation of prostates	409 sq.
- in skin, hair and nails	520
- sulphate, decormal solutions	277
- in sweat	680
- in transcarboxylic acid cycle	390, 391
- in urine	664
Manganese-52 and -54, characteristics .	292
- decay table	296
D-Mannohexitose	311
Mannosamine, formation	423
D-Mannose (Man)	310, 315
- in serum glycoproteins	606
- 1 phosphate, in L-fucose formation .	423
- as guanonic diphosphate mannose from	329
- 6 phosphate	423
- in L-fucose formation	673
- in urine	684
Mannosidases in seminal plasma	
MAO. See Monoamine oxidase	
Maple syrup urine disease	448, 449
Mare's milk, composition	511
Margaric acid	367
Margarine, composition	510
Marrow, bone. See Bone marrow	
Mass energy transfer coefficient	218, 220
Mass numbers	217
Mass stopping power	218
Mass units	204, 205
Mastocytosis I, urinary histidine metabolites	670
Mathematical constants	9
- symbols	132
Maxwell	216
Mayergass, composition	310
NBC (maximum breathing capacity) . .	543
McArdle's syndrome	430, 431
MCHf (mean corpuscular haemoglobin)	613, 617
MCHC (mean corpuscular haemoglobin	
concentration)	576, 615, 617
MCV (mean corpuscular volume)	614, 615, 617
Md (muscle levium)	243
MDH1. See Maleate dehydrogenase	
Meson day	137
Mesles anti-scuro, reference preparation	761
Mest, amino acids	516
- composition	511 sq.
- vitamin losses during cooking	498
Mecuron, composition and properties .	657 sq.
- pregnenolol	754
Mediterranean anaemia	9
MEFR. See Expiratory flow rate, maximum	
mega- (10 ⁶)	9
Megakaryocytes in bone marrow	621
Megaloblastic anaemia. See under Anaemia	
Melanin, formation from tyrosine	440, 722
- function	722
- lack	448
- in urine	661
Melanocytes, effect of melanotropin . .	722
Melanocyte-stimulating hormone	721, 722
- gonadotropins	714
- iron requirement	496
- oestradiol formation	755
- plasma, amino acids	574
- androgens	751
- ascorbic acid	611
- urine, amino acids	667
- citric acid	674
- creatine	673
- glucuronic acid	685
- gonadotropins	714
- 3 hydroxy-kynurenine	669
- melatonin	722
- 1-methyl 2 pyridones 5-carboxylamide	676
- estrogens	756, 757
- pregnandiol	754
- statosteroids	752
Meraptans in urine	663
Merapturic acids	330
- in detoxication	445
Mercuric chloride, decormal solutions .	277
Mercury, in blood	367
- dairy	230
- flame lines	411
- inhibition of aminopeptidase	642
- properties, isotopes, etc	252
Mercury-197, characteristics	293
- decay table	305, 306
- diagnostic use	289
Mercury-198, vacuum wave lengths . .	200
Mercury 203, characteristics	293
- decay table	306
Mercury barometer correction	255
Mercury dihalides, effect on thymus	
sarcoma	676
Mesoblene (Cy)	362, 363
Mesoblerhythm	364
Mesobifucetide	364
- in faeces	364
Mesobibibodm	637
Mesobibubidin	364
Mesobibubigen	362, 363
Mesobibubiolin	362, 363
Meso compounds	364
Mesomental	309
- in plasma	361
- in urine	322, 403
Mesoporphyrin	605
- in faeces	673
Mesothorium I, properties	358
Mesothorium II, properties	649
Misotocin	245
Messenger RNA. See under RNA	
Mst. See 2-Methoxy-	

- Metabolic acidosis and alkalosis 528
 - body size 473
 - diseases, congenital 446 sq.
 - quotients 387, 388
 - rate, basal (BMR). See Basal metabolism
 - resting (RMR) 495
 - reactions 389 sq.
 Metabolism 387 sq.
 - basal. See Basal metabolism
 - cell 387, 388
 - of erythrocytes 616
 - inborn errors 446 sq.
 - of leucocytes 618
 - of lipids. See under Lipids
 - mineral. See Electrolyte balance
 - of plasma proteins 579
 - of thrombocytes 621
 Metamorphosis test 727
 Metamyelocytes in bone marrow 621
 Metanephrine in urine 668, 733
 Metanil yellow indicator 283
 Metaphosphatases 405
 Meter. See Metre
 Methaemoglobin 359, 360
 - acid 359
 - alkaline 359
 - in blood 576
 Methaemoglobinemia 576
 - congenital 447
 Methanoic acid 366
 L-Methionine (Met) 332
 - biosynthesis 479
 - from homocysteine 437
 - vitamin B₁₂ in 485
 - in blood 574
 - in blood proteins 581
 - cell constituents from 434
 - creatine from arginine, glycine and 437
 - degradation 398, 402
 - dietary requirements 496
 - in foods 516
 - in milk 688
 - in saliva 645
 - in urine 667
 Methionylkallidin 742
 Methionyl-lysylthiopyridine 742
 Methoxyestr. See Methoxyestr.
 3-Methoxy-4-hydroxymandelic acid, from catecholamine breakdown 732
 - in urine 675, 733
 3-Methoxy-4-hydroxy- β -phenylacetaldehyde from catecholamine breakdown 732
 3-Methoxy-4-hydroxyphenylacetic acid, from catecholamine breakdown 732
 - in urine 675
 3-Methoxy-4-hydroxy- β -phenylethanol from catecholamine breakdown 732
 3-Methoxy-4-hydroxyphenylglycol, from catecholamine breakdown 732
 - in urine 675
 3-Methoxy-4-hydroxyphenylglycolaldehyde from catecholamine breakdown 732
 2-Methoxyoestrone in urine 756
 2-Methoxyoestrone, biosynthesis and metabolism 431
 - in urine 756
 - in pregnancy 757
 5-Methoxytryptamine in urine 669
 Methoxytyramine from catecholamine breakdown 732
 α -Methylacetoacetyl-coenzyme A in isoleucine degradation 396
 Methylacrylyl-coenzyme A in valine degradation 396
 2-Methyladeninecyanoamide 483
 2-Methyladenosine 354
 2'-O-Methyladenosine 354
 N⁶-Methyladenosine 354
 5-Methyladenosylmethionine in oestrogen metabolism 431
 N-Methyladrenaline, breakdown 732
 α -Methyl- β -alanine. See β -Aminoisobutyric acid
 Methylamine in urine 668
 5-Methyl-6-amino-2-hydroxypyrimidine 338
 Methylaspartate mutase, vitamin B₁₂ 485
 Methylation in detoxication 442 sq.
 5-Methylbenzimidazolylcyanocobamide 483
 2-Methyl-1,2-bis-(3-pyridyl)-1-propanone (metyrapone) test 717
 3-Methylbutanoic acid 371
cis-2-Methyl- Δ^2 -butenoic acid 371
 α -Methylbutyryl-coenzyme A in isoleucine degradation 396
 α -Methylcarbamyl- β -alanine in thymine degradation 401
 24-Methyl-5 α -cholestane in steroids 381
 24-Methylcholesta-5,7,22-trien-3 β -ol. See Ergosterol
 Methylcobalamin 482, 483, 485
 - in serum 484, 610
 β -Methylcrotonyl-CoA-carboxylase, biotin 487
 β -Methylcrotonyl-coenzyme A in leucine degradation 395
 2'-O-Methylcytidine 354
 3-Methylcytidine 354
 5-Methylcytidine 354
 5-Methylcytosine 338
 Methylene group, mol. wt. multiples 250
 5,10-Methylenetetrahydrofolic acid, in transfer of one-carbon groups 436, 437
 - in synthesis of purines and methionine 479
 - in pyrimidine synthesis 439
 5,10-Methylenetetrahydropteroylglutamic acid. See 5,10-Methylenetetrahydrofolic acid
 N-Methyl-L-glucosamine 315
 β -Methylglutacetyl-coenzyme A in leucine degradation 395
 1-Methylglycocyanine. See Creatinine
 Methylglycocyanine. See Creatine
 Methyl group, mol. wt. multiples 250
 Methylguanidine, in blood 573
 - in urine 666
 1-Methylguanine in urine 671
 Methylguanoses 354
 1-Methylguanosine 354
 14-Methylhexadecanoic acid 371
 1-Methylhistidine 335
 - in blood 574
 - in urine 667
 3-Methylhistidine 335
 - in blood 574
 - in urine 667
 α -Methyl- β -hydroxybutyryl-coenzyme A in isoleucine degradation 396
 1-Methylhypoxanthine in urine 671
 5,10-Methylidynetetrahydrofolic acid, in L-histidine degradation 395
 - in inosinic acid formation 433
 - in transfer of one-carbon groups 436, 437
 - in synthesis of purines and methionine 479
 1,4-Methylimidazoleacetic acid in urine 670
 1-Methylinosine 354
 Methylmalonic acid in urine 449, 674
 Methylmalonic semialdehyde, from α -methyl- β -alanine 401
 - in valine degradation 396
 Methylmalonyl-CoA carboxyltransferase, biotin in 487
 Methylmalonyl-CoA mutase, in degradation of fats 392
 - vitamin B₁₂ 485
 Methylmalonyl-CoA racemase in degradation of fats 392
 Methylmalonyl-coenzyme A in degradation of fats 392
 N-Methylmetanephrine from catecholamine breakdown 732
 Methylmaphthoquinone 468
 N₁-Methylnicotinamide. See 1-Methyl-nicotinamide
 1-Methylnicotinamide 477
 - in plasma 610
 - in urine 676
 D-[J]-10-Methyloctadecanoic acid 371
 Methyl orange indicator 283
 6 α -Methylprednisolone 380
 - biological activity 750
 2-Methylpropanoic acid 371
 2'-O-Methylpseudouridine 354
 N₁-Methyl-2-pyridone-5-carboxylamide 477
 - in urine 676
 1-Methyl-4-pyridone-5-carboxylamide in urine 676
 1-Methyl-6-pyridone-3-carboxylamide. See N₁-Methyl-2-pyridone-5-carboxylamide
 Methyl red indicator 283
 24-Methyl-9,10-secocholesta-5,7,10(19),22-tetraen-3 β -ol. See Vitamin D₄
 β -Methylserine. See L-Threonine
 Methyltestosterone, biological activity 752
 5-Methyltetrahydrofolate homocysteine transmethyle, vitamin B₁₂ in 485
 5-Methyltetrahydrofolic acid 481
 - in blood 610
 - in whole body 479
 - in methionine formation 437
 - in transfer of one-carbon groups 436, 437
 5-Methyltetrahydrofolic acid, in synthesis of purines and methionine 479
 5-Methyltetrahydropteroylglutamic acid. See 5-Methyltetrahydrofolic acid
 5-Methyl-THF. See 5-Methyltetrahydrofolic acid
 8-Methyltolcol 465
 8-Methyltocotrienol 465
 Methyltransferases 385
 O-Methyltransferase in oestrogen metabolism 430
 13-Methyltridecanoic acid 371
 6 α -Methyl-11 β ,17 α ,21-trihydroxypregna-1,4-diene-3,20-dione. See 6 α -Methylprednisolone
 Methyluridines 354
 Metre 200
 Metre-kilogramme-second-ampere system 215, 216
 Metric ton 204
 Metyrapone test 717
 Mevalonic acid, in cholesterol synthesis 426, 427
 - in synthesis of ubiquinones 466
 Mevalonyl phosphate in cholesterol synthesis 426, 427
 - pyrophosphate in cholesterol synthesis 426, 427
 - ribophosphate in cholesterol synthesis 426, 427
 Mg. See Magnesium
 Mho 216
 mi (mile) 200
 MICHAELIS constant 382 sq.
 micro- (10⁻⁶) 9
 Microbar 211, 212
 Microcytic anaemia 448
 Micrometre 200
 Micron 200
 Mid-expiratory flow, maximum (MMF) 543
 - determination 549
 MIFR (inspiratory flow rate, maximum) 543
 Mil 200
 - circular 203
 - mile, geographical 200
 - nautical 200
 - statute 200
 Milk, breast (see also Breast feeding) 687 sq.
 - amino acids 516, 688
 - fat content variations 687
 - fatty acids 687
 - alkaline phosphatase 470, 689
 - thiamine 457, 689
 - vitamin A 687
 - yield 687 sq.
 - cow's 516, 688
 - amino acids 663, 664
 - effect on urinary electrolytes 687
 - fatty acids 666
 - effect on urinary nitrogen 666
 - effect on infants' stools 511
 - dietary data 723
 - ejection, effect of oxytocin 689
 - oligosaccharides 347, 350, 424
 - formation 419
 - xanthine oxidase 9
 milli- (10⁻³) 211, 212
 Millibar 200
 Millimetre 212
 - of mercury 212
 - of water 200
 Millimicron 204
 min (minim) 205
 min (minute) 205
 Mineral metabolism. See Electrolyte balance
 Mineralocorticoids 379 sq., 428, 748 sq.
 - determination 743
 Mineralocorticosteroids. See Mineralocorticoids
 Minim 204
 Minute 206
 Minute (angle) 207, 208
 Minute ventilation (l τ) 542, 550
 Minute volume of pulmonary circulation 544
 Mitochondria, vitamin B₁₂ 543
 Mixing time in lung-spirometer system 543
 MK (myokinase). See Adenylate kinase
 MKSA (metre-kilogramme-second-ampere) units 215, 216
 MMF. See Mid-expiratory flow, maximum
 mmHg (millimetre of mercury) 212
 mmH₂O (millimetre of water) 212
 Mn. See Manganese
 MNs blood-group system 633
 - clinical significance 490
 Mo. See Molybdenum
 MOTTLER-BARLOW disease 226, 227, 270
 mol (mole) 226, 227, 270

- Newborn (*rand*), erythrocytes, count . . . 614, 617
 - diameter . . . 617
 - glutathione . . . 573
 - lifetime . . . 616
 - osmotic resistance . . . 616
 - sedimentation rate . . . 558, 559
 - mean corpuscular volume . . . 615, 617
 - faeces, composition and properties . . . 657 sq.
 - fat weight . . . 517
 - functional residual capacity . . . 542
 - gastric juice, acidity . . . 648
 - pH . . . 647
 - haematocrit . . . 614, 617
 - haemolytic jaundice . . . 577, 632
 - composition of hair and nails . . . 520
 - iodide metabolism . . . 726
 - leucocyte count . . . 618, 619
 - lung values . . . 550
 - normal measurements . . . 692, 693
 - muscle, composition . . . 518
 - weight . . . 517
 - organs, composition . . . 519
 - weights . . . 710
 - pulmonary compliance . . . 545
 - respiratory quotient . . . 539
 - reticulocytes . . . 612, 613
 - saliva, amylase . . . 646
 - volume . . . 643
 - skin, composition . . . 521
 - daily number of stools . . . 657
 - sweat electrolytes . . . 679, 680
 - teeth, composition . . . 521
 - development . . . 709
 - thiamine . . . 470
 - organic components of tissues . . . 522
 - under-weight, weight gain . . . 692
 - urinary concentration . . . 662
 - urine, acidity . . . 662
 - amino acids . . . 666, 667
 - ammonia . . . 666
 - calcium . . . 664
 - carbohydrates . . . 673
 - catecholamines . . . 733
 - chloride . . . 662
 - corticosteroids . . . 746 sq.
 - creatine . . . 665
 - creatinine . . . 665
 - erythrocytes . . . 677
 - guanidinocetic acid . . . 666
 - leucocytes . . . 677
 - magnesium . . . 664
 - nitrogen . . . 665
 - oestriol . . . 756
 - phosphorus . . . 663
 - potassium . . . 663
 - proteins . . . 668
 - specific gravity . . . 661
 - sulphur . . . 663
 - urea . . . 665
 - uric acid . . . 671
 - vitamins . . . 676
 - volume . . . 661
 - vital capacity . . . 542
 - vitamin A prophylaxis . . . 460
 - vitamin A requirement . . . 460
 - vitamin E deficiency . . . 466
 - vitamin K therapy . . . 468
 - water requirement . . . 524
 - weight . . . 692, 693
 Newcastle disease antiserum, reference
 - preparation . . . 761
 - vaccine, standard and reference preparation . . . 759
 Newton . . . 211, 216
 Ni. See Nickel
 Niacin. See Nicotinic acid
 Niacinamide . . . 477
 Nickel, flame lines . . . 284
 - properties, isotopes, etc. . . 236
 - in urine . . . 664
 Nicotinamide . . . 477
 Nicotinamide mononucleotide (NMN) . . . 344
 Nicotinamide-adenine dinucleotide (NAD;
 in reduced form NADH, NADH₂) . . . 344, 477
 - in alcoholic fermentation . . . 390
 - in biological oxidations . . . 403
 - in blood . . . 577
 - enzymatic cleavage . . . 416
 - in L-cysteine degradation . . . 397
 - in degradation of fats . . . 392, 393
 - formation from nicotinic acid . . . 477
 - functions . . . 477
 - in glutamic acid formation . . . 432
 - in glycolysis . . . 389
 - in hydroxyproline formation . . . 432
 Nicotinamide-adenine dinucleotide, in
 isoleucine degradation . . . 396
 - in leucine degradation . . . 395
 - in methionine formation . . . 479
 - in norleucine degradation . . . 396
 - in transfer of one-carbon groups . . . 437
 - in proline formation . . . 432
 - in purine formation . . . 479
 - in pyrimidine formation . . . 439
 - in serine degradation . . . 397
 - in oxidation of sugars . . . 391
 - in L-threonine degradation . . . 397
 - in tricarboxylic acid cycle . . . 390, 391
 - in UDP-glucuronic acid formation . . . 423
 - in UDP-iduronic acid formation . . . 423
 - in urea synthesis . . . 444
 - in valine degradation . . . 396
 - in xanthylic acid formation . . . 436
 Nicotinamide-adenine dinucleotide phosphate
 (NADP; in reduced form NADPH,
 NADPH₂) . . . 344, 477
 - in blood . . . 577
 - in carbon-chain extension . . . 424
 - in cholesterol synthesis . . . 426
 - enzymatic cleavage . . . 416
 - in degradation of fats . . . 392
 - in fatty acid synthesis from citrate . . . 424, 425
 - formation, from nicotinic acid . . . 477
 - in pentose phosphate cycle . . . 422
 - functions . . . 477
 - in glutamic acid formation . . . 432
 - in methionine formation . . . 479
 - in transfer of one-carbon groups . . . 437
 - in phenylalanine-tyrosine conversion . . . 439
 - in purine formation . . . 479
 - in tricarboxylic acid cycle . . . 390, 391
 Nicotinic acid . . . 476 sq.
 - in blood . . . 477, 610
 - in cerebrospinal fluid . . . 639
 - deficiency . . . 478
 - dietary requirements . . . 478, 493
 - in foods . . . 499 sq.
 - losses during cooking . . . 498
 - conjugation with glycine . . . 444
 - in liver . . . 477
 - in milk . . . 689
 - NAD formation from . . . 477
 - in tryptophan degradation . . . 398, 399, 475
 - in urine . . . 477, 676
 Nicotinic acid adenine dinucleotide in NAD
 and NADP formation . . . 477
 Nicotinic acid mononucleotide in NAD and
 NADP formation . . . 477
 Nicotinic acid . . . 477
 NIEMANN-PICK disease . . . 455, 456
 Ninhydrin . . . 329
 Ninhydrin reaction . . . 573
 Niobium, flame lines . . . 284
 - properties, isotopes, etc. . . 237
 Nisinic acid . . . 370
 Niton, properties, isotopes, etc. . . 244
 Nitramine indicator . . . 283
 p-Nitraniline, acetylation . . . 444
 Nitrate in urine . . . 664
 Nitric acid, decinormal solutions . . . 277
 Nitrite, in blood . . . 564
 - in urine . . . 664
 Nitritocobalamin . . . 482
 Nitrogen, atomic weight multiples . . . 250
 - in blood . . . 572
 - determination . . . 568
 - in whole body . . . 517
 - in bones and teeth . . . 521
 - in foods . . . 498 sq.
 - in leucocytes . . . 572
 - in muscle . . . 518
 - nonprotein. See Nonprotein nitrogen
 - in organs . . . 519
 - in placenta and amniotic fluid . . . 522
 - properties, isotopes, etc. . . 234
 - in skin, hair and nails . . . 520
 - in thrombocytes . . . 572
 Nitrophenol indicators . . . 283
 Nitrous acid (*see also* Nitrite), decinormal
 solutions . . . 277
 nmile (nautical mile) . . . 200
 NMN (nicotinamide mononucleotide) . . . 344
 No (nobelium) . . . 248
 Nobelium, properties and isotopes . . . 248
 Nodules . . . 353
 Noise levels . . . 225, 226
 Nomogram, acid-base balance of blood . . . 569
 - aortic diameter and biological age . . . (inside
 back cover)
 Nomogram, blood, plasma and erythrocyte
 volumes . . . 556
 - body surface area . . . 537, 538
 - serum cation concentration . . . 562
 - drops per minute . . . 529
 - HENDERSON-HASSELBALCH formula . . . 528
 - lung values . . . 547, 550
 Nonacosanoic acid . . . 367
 Nonadecanoic acid . . . 367
 Nonanoic acid . . . 366
 Nondecylic acid . . . 367
 Nonoses . . . 316
 Nonprotein nitrogen (NPN), in bile . . . 654
 - in blood . . . 572, 683
 - in cerebrospinal fluid . . . 636
 - in gastric juice . . . 649
 - in milk . . . 511, 683
 - in pancreatic juice . . . 652
 - in saliva . . . 645
 - in synovial fluid . . . 641
 - in tissues . . . 522
 Nonsecretors of ABH substances . . . 631
 Noodles, composition . . . 508
 Noradrenaline . . . 730
 - breakdown . . . 732
 - formation from tyrosine . . . 440, 731
 - in plasma . . . 731, 733
 - release . . . 731
 - in urine . . . 668, 733
 Noradrenochrome from noradrenaline . . . 731
 Nor-compounds . . . 381
 Norpinephrine. See Noradrenaline
 Northandrolone . . . 380
 Norethindrone . . . 380
 Norethisterone . . . 380
 Norethynodiol . . . 380
 Norleucine . . . 332
 - degradation . . . 396, 402
 Normal distribution (*see also* Index,
 pages 197-198) . . . 161 sq., 169 sq.
 'Normal' format . . . 133
 Normal solutions of reagents . . . 277
 Normal temperature and pressure (NTP) . . . 260
 Normality, temperature variation . . . 251
 Normetanephrine, from catecholamine
 breakdown . . . 732
 - in urine . . . 668, 733
 Normoblasts . . . 612
 Normoline degradation . . . 396, 402
 Novobiocin, standard . . . 761
 Np (neptunium) . . . 248
 NPN. See Nonprotein nitrogen
 Nt (niton) . . . 260
 NTP (normal temperature and pressure) . . . 229
 Nuclear magnetron . . . 406, 418, 419
 Nucleases . . . 406, 418, 419
 Nucleic acids . . . 351 sq.
 - biosynthesis from pentose phosphates . . . 578
 - in leucocytes . . . 534
 - minor constituents . . . 329
 Nucleoproteins . . . 684
 - in semen . . . 336, 337, 339 sq.
 Nucleosides . . . 336, 337, 339 sq.
 - enzymatic cleavage . . . 406, 418, 419
 - minor . . . 336
 Nucleoside diphosphate kinase . . . 339, 740
 Nucleoside kinases . . . 336
 Nucleoside monophosphate kinase . . . 343
 Nucleoside phosphates . . . 343
 Nucleosidephosphate kinase in pyrimidine
 synthesis . . . 450
 Nucleotidases . . . 401
 5'-Nucleotidase . . . 507
 - in plasma . . . 409
 - in purine degradation . . . 336, 337, 342 sq.
 Nucleotides . . . 336, 337, 342 sq.
 - biosynthesis . . . 325 sq.
 - in blood . . . 344 sq.
 - with coenzyme functions . . . 410
 - enzymatic cleavage . . . 338 sq., 406, 418, 419
 - in erythrocytes . . . 416
 Nucleotide pyrophosphatase . . . 386
 Nucleotidyltransferases . . . 217
 Nuclides . . . 226
 - relative atomic masses . . . 234 sq.
 - natural, properties . . . 234 sq.
 - radioactive. See Radionuclides
 Numbers, definitions . . . 131
 - random . . . 493 sq.
 Nutritional standards . . . 468 sq.
 - tables . . . 516
 Nuts, amino acids . . . 417
 - composition . . . 761
 Nystatin, standard . . . 761

[illegible]

A detailed index to the statistical tables (pages 28–131) and chapter on Statistical Methods (pages 146–196) will be found on pages 197–198

- Palmitoleic acid (*contd.*), in serum lipids. 604
 Pancreas, composition. 508
 Pancreas, ascorbic acid. 490
 – beef, composition. 512
 – effect of cholecystokinin-pancreozymin. 739
 – cystic fibrosis, salivary calcium. 644
 – salivary chloride. 643
 – salivary nitrogen. 645
 – salivary sodium. 644
 – serum tocopherols. 609
 – sweat electrolytes. 680
 – sweat iodine. 679
 – sweat toxicity. 679
 – vitamin E. 467
 – disease, serum α -amylase. 597
 – serum enzyme changes. 587
 – serum β -glucuronidase. 597
 – DNases. 418
 – enzyme activities. 585
 – fatty acid esterases. 414
 – insulin content. 735
 – lactic acid fermentation. 388
 – phospholipases. 417
 – proteolytic enzymes. 408, 409
 – proteolytic enzyme precursors. 407
 – respiratory rate. 387
 – RNAase. 418
 – effect of secretin. 739
 – weight. 710
 Pancreatic juice. 651 sq.
 – amount. 525, 651
 – electrolytes. 525, 652
 – glycosidases. 411, 412
 Pancreatitis, faecal trypsin and chymotrypsin. 659
 – serum enzyme changes. 587
 – serum lipase. 595
 Pancreatopeptidase E. 408
 – in pancreatic juice. 652
 Pancreozymin. 651, 739
 Pancreozymin test. 652, 653
 Panose, hydrolysis. 412
 Pantethin. 488
 – in coenzyme A formation. 487
 Panthenol. 488
 Pantole acid in pantothenic acid synthesis. 487
 Pantothenic acid. 487, 488
 – in blood. 488, 611
 – in cerebrospinal fluid. 488, 639
 – in coenzyme A. 345, 487, 488
 – deficiency. 488
 – dietary requirements. 488
 – in foods. 499 sq.
 – in liver. 488
 – in milk. 689
 – in urine. 488, 676
 Pantothényl alcohol. 488
 N-Pantothényl- β -aminoethanethiol. See
 Pantethin
 N-Pantoyl-3-propanolamine. 488
 Para-aminohippuric acid (PAH). See
 β -Aminohippuric acid
 – hydrogen. 359
 – virus antisera, reference. 247
 – reagents. 764
 Parallelepiped, geometry. 142
 Parallelogram, geometry. 142
 Parapepsin. 407
 Paraproteins. 581
 – in erythrocyte sedimentation. 559
 Parathormone. See Parathyroid hormone
 Parathyroid hormone. 728
 – vitamin D and. 461
 Parietal secretion of gastric juice. 647
 Paromomycin, reference preparation. 762
 Parotid saliva. See Saliva
 Parsec. 201
 Parsley, composition. 505
 Parsnips, composition. 505
 PASTEUR effect. 387
 Pb. See Lead
 P blood-group system. 627, 628
 – clinical significance. 633
 pc (parsec). 201
 PCV (packed cell volume). See Haematocrit
 Pd. See Palladium
 pdl (poundal). 211
 Peas, amino acids. 516
 – composition. 505
 Peaches, composition. 501
 Peak flow rate. See Expiratory flow rate,
 maximum
 Peanuts, amino acids. 516
 – composition. 507
 Peanut butter, composition. 510
 – oil, composition. 510
 Pears, composition. 501
 Pecans, composition. 507
 Peck. 204
 Peptic acid. 328
 Peetins. 328
 Pelargonie acid. 366
 Pellagra. 478
 Pelvic width during growth. 695 sq.
 Penicillin K, reference preparation. 762
 Pennyweight. 205
 Pentacosanoic acid. 367
 Pentadecanoic acid. 367
 Pentadecylle acid. 367
 Pentane acids in serum lipids. 604
 Pentanoic acid. See *n*-Valeric acid
 Pentoses. 308, 313, 314
 – degradation. 399
 – nucleotide, in erythrocytes. 605
 – in plasma. 605
 Pentose 5-phosphates in erythrocytes. 605
 Pentose phosphate cycle. 389, 420 sq.
 – in degradation of pentoses. 399
 Pentosuria. 451
 Pentosyltransferases. 386
 Peppers, composition. 505
 Pepsin. 407
 – formation from pepsinogen. 406
 – in gastric juice. 650
 – inhibitor. 406
 – in plasma. 598
 Pepsin B. 407
 Pepsinogen. 406
 – gastric secretion. 647
 Peptidases. See Peptide hydrolases
 Peptide hydrolases. 386, 405 sq.
 – in milk. 689
 Peptides, enzymes hydrolysing. 406 sq.
 – in urine. 666
 Peptide nitrogen, in bile. 654
 – in gastric juice. 649
 Peptide synthetases. 386
 Peptidyl-amino-acid hydrolases. 386, 405, 408, 409
 Peptidyl-peptide hydrolases. 386, 405 sq.
 Perch (unit). 200
 Perch, composition. 515
 Pericarditis, serum enzyme changes. 587
 Period (periodic time). 225
 Periodic system of the elements. 231
 Pernicious anaemia. See under Anaemia
 Peroxidases. 361, 362
 – in milk. 689
 – in thyroid hormone formation. 440, 726
 Peroxide haemolysis test. 466
n-Perseulose. 311
 Persimmons, composition. 501
 Pertussis vaccine, standard. 759
 Petroselinic acid. 369
 PFA (phosphofructaldolase). See Ketose-
 1-phosphate aldolase
 PGDH. See Phosphogluconate dehydro-
 genase
 PGE, PGF. See Prostaglandins
 PGK. See Phosphoglycerate kinase
 PGluM. See Phosphoglucomutase
 PGM. See Phosphoglycerate phosphomutase
 pH value. 278
 – of bile. 654
 – of body fluids. 527
 – of buffers. 280 sq.
 – of cerebrospinal fluid. 635
 – and enzyme action. 382
 – of faeces. 657
 – of gastric juice. 647
 – of intestinal juice. 656
 – of milk. 688
 – of pancreatic juice. 651
 – of saliva. 643
 – of semen. 682
 – standards. 278, 279
 – of sweat. 679
 – of synovial fluid. 640
 – of urine. 662
 PHI (prolactin hormone). See Prolactin
 Phagocytes in synovial fluid. 640
 Phe. See L-Phenylalanine
 Phenacetylglutamine. See Phenylacetylglut-
 amine
 Phenol in urine. 675
 Phenols, conjugation. 442
 – esterification as sulphate. 445
 – in faeces. 659
 – in urine. 675
 Phenolic acids in coffee. 509
 Phenolphthalein indicator. 283
 Phenol red indicator. 283
 Phenolsulphonphthalein (PSP) test. 532, 533
 Phenotypes, blood-group. 626 sq.
 Phenylacetic acid, detoxication. 445
 Phenylacetyl-coenzyme A in detoxication of
 phenylacetic acid. 445
 Phenylacetylglutamine, formation. 445
 – in urine. 666
 L-Phenylalanine (Phe). 332
 – accumulation. 443
 – in blood. 448, 574
 – in blood proteins. 581
 – in cerebrospinal fluid. 448
 – decarboxylation. 394
 – degradation. 398, 402
 – dietary requirements. 496
 – in foods. 516
 – in milk. 688
 – in saliva. 645
 – in sweat. 680
 – conversion to tyrosine. 439
 – in synthesis of ubiquinones. 466
 – in urine. 667
 Phenylalanine 4-hydroxylase, in phenyl-
 alanine degradation. 398
 – in phenylketonuria. 448
 Phenylethanolamine *N*-methyltransferase in
 adrenaline and noradrenaline formation. 440
 Phenylethylamine, formation from
 phenylalanine. 394
 Phenylketonuria. 448, 449
 Phenylpyruvic acid in urine. 448
 PHI (phosphohexose isomerase). See
 Glucosephosphate isomerase
 Phon. 225
 Phosphatases. 405, 415, 416
 Phosphatase, acid. 415
 – allotypy. 634
 – in bile. 655
 – isozymes. 584
 – in milk. 689
 – in plasma. 585, 596
 – effect of muscular work. 586
 – in saliva. 645
 – in semen. 684
 – in synovial fluid. 641
 – units and conversion factors. 584
 – in urine. 672
 – alkaline. 415
 – in bile. 655
 – and bone growth in children. 585
 – in gastric juice. 650
 – isozymes. 584
 – in milk. 689
 – in plasma. 415, 596
 – in heart disease. 587
 – in liver disease. 586, 587
 – effect of muscular work. 586
 – in pregnancy. 586
 – in saliva. 645
 – in semen. 684
 – in synovial fluid. 641
 – units and conversion factors. 584
 – in urine. 672
 – in fructose formation. 411
 – interconversion of glycogen
 phosphorylase. 473
 – in vitamin B₆ interconversions. 473
 Phosphate (see also Phosphoric esters and Phos-
 phorus), in biological energy trans-
 formations. 404
 – in blood, buffer capacity. 432
 – inborn disturbance. 523
 – in body fluids. 280 sq.
 – buffers. 523
 – conversion factors. 251, 274 sq.
 – in DNA synthesis. 453, 663
 – excretion. 729
 – calcitonin and. 663
 – index. 728
 – parathyroid hormone and. 649
 – in gastric juice. 536
 – glomerular filtration and excretion. 365
 – in lipids. 652
 – in pancreatic juice. 679
 – in sweat. 641
 – in synovial fluid. 677, 678
 – in urinary sediments. 376
 Phosphatidyl ethanolamine. 375 sq.
 Phosphatides. 456
 – accumulation. 654, 658
 – in bile. 654, 658

[illegible]

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- Plasma (cont'd), angiotensin 741
- arginine 598
 - ascorbic acid 490, 611
 - aspartate aminotransferase 593
 - bicarbonate 562, 571
 - blood acid-base balance and 569
 - bile acids 601
 - bilirubin 362, 576, 577
 - in metabolic disease 454
 - biotin 611
 - bradykinin 742
 - bromide 563
 - buffer capacity 527
 - caeruloplasmin 583, 593
 - calcitonin 729
 - calcium 565
 - calcitonin and 729
 - carbonic acid, blood acid-base balance and 569
 - carnitine 573
 - carotenes 457, 609
 - cations 561
 - nomogram 562
 - cephalin 604
 - chenodeoxycholic acid 601
 - chloride 562
 - cholesterol 456, 600, 601, 603, 604
 - cholesterol esterase 414
 - choline 575
 - cholinesterase 414, 595
 - chorionic gonadotropin 715
 - chylomicrons 602
 - citric acid 607
 - cobalt 566
 - colloid-osmotic pressure 526, 558
 - copper 566
 - coproporphyrin 575
 - corticosteroids 745
 - protein binding 428
 - corticosterone 745
 - cortisol 716, 745
 - cortisone 745
 - creatine 572
 - creatine kinase 594
 - creatinine 531, 572
 - and glomerular filtration rate 531, 532
 - dehydroascorbic acid 611
 - dehydroepiandrosterone sulphate 752
 - dehydrogenases 590 sq.
 - deoxycholic acid 601
 - 11-deoxycortisol 745
 - deoxyribonucleases 597
 - dextran expanders 530
 - dihydrocholesterol 601
 - dihydroxycholic acids 601
 - dry substance 561
 - electrolytes 523
 - conversion factors 523
 - enzymes 585 sq.
 - allotypy 634
 - maintenance 585
 - enzyme activity gradients between tissue and 586
 - ergothioneine 573
 - erythropoietin 740
 - ethanolamine 573
 - fats 374
 - fatty acids 600, 601, 603, 604
 - fibrinogen 579, 582
 - flavinadenine dinucleotide 609
 - flavin mononucleotide 609
 - flow rate, into small intestine 656
 - into stomach 650
 - fluoride 563
 - folic acid 479, 610
 - folinic acid 479
 - freezing-point depression 526, 557
 - fructosediphosphate aldolase 599
 - fucose 606
 - fumarate hydratase 599
 - globulin fractions 582, 583
 - glucose 605
 - osmotic activity 526
 - glucose-6-phosphatase 597
 - glucose-6-phosphate dehydrogenase 592
 - glucosephosphate isomerase 600
 - glucuronic acid 605
 - β -glucuronidase 597
 - glutamate dehydrogenase 592
 - glutathione reductase 592
 - glyceraldehyde phosphate dehydrogenase 592
 - glycerol 607
 - glycerophosphate dehydrogenase 590
 - glycolaldehydetransferase 593
 - glycoproteins 606
- Plasma, glyoxalic acid 607
- growth hormone 719, 720
 - guanidinoacetic acid 573
 - guanine deaminase 598
 - haemoglobin 576
 - haemoglobin excretion and 671
 - α_1 -haptoglobin 583
 - heparin 606
 - hexokinase 594
 - hexosamines 606
 - hexoses 606
 - histamine 575
 - α -hydroxybutyrate dehydrogenase 591
 - β -hydroxybutyric acid 608
 - 17-hydroxycorticosteroids 745
 - hydroxyprogrenones 754
 - 17 α -hydroxyprogesterone 754
 - hypoxanthine 577
 - L-iditol dehydrogenase 590
 - indolyl-3-acetic acid 575
 - indolyl-3-lactic acid 575
 - 3-indoxylsulphuric acid 575
 - insulin 735, 736
 - iodine 564, 726
 - iron 566
 - iron-binding capacity 566
 - isocitrate dehydrogenase 591
 - ketohexokinase 594
 - ketose-1-phosphate aldolase 599
 - Δ^4 -3-ketosteroids 745
 - kinins 742
 - lactate dehydrogenase 590
 - lead 567
 - lecithin 604
 - leucine aminopeptidase 598
 - lipase 595
 - lipids 600 sq.
 - fatty acid composition 604
 - in pregnancy and post partum 691
 - lipid phosphorus 563
 - lipoic acid 608
 - lipoproteins 583, 602
 - lithium 567
 - lysolecithin 604
 - α_2 -macroglobulin 583
 - magnesium 566
 - malate dehydrogenase 591
 - malic acid 607
 - manganese 567
 - melanotropins 722
 - mesoinositol 605
 - methylcobalamin 484, 610
 - 1-methylnicotinamide 610
 - 5-methyltetrahydrofolic acid 479
 - molarity and molality 271
 - myoglobin, myoglobin excretion and 671
 - nicotinic acid 477, 610
 - nitrogen 572
 - nonprotein nitrogen 572
 - and glomerular filtration rate 531, 532
 - and renal inulin clearance 532
 - noradrenaline 731, 733
 - 5'-nucleotidase 597
 - nucleotides 577
 - oestrogens 756
 - oncotic pressure 526
 - ornithine carbamoyltransferase 593
 - osmolarity 271, 526, 557
 - and urinary concentration 533
 - osmotic pressure 526, 557
 - oxalic acid 607
 - oxytocin 723
 - oxytocinase 598, 723
 - pantothenic acid 611
 - parathyroid hormone 728
 - pentoses 605
 - pepsin 598
 - pH value 560
 - and blood acid-base balance 569
 - phosphatases, phosphoethanolamine excretion and 668
 - acid phosphatase 596
 - alkaline phosphatase 596
 - in bone destruction 415
 - phosphate 563
 - inborn disturbance 452
 - phosphatides 601, 604
 - phosphoethanolamine 573
 - phosphoglucomutase 595
 - phosphogluconate dehydrogenase 591
 - phosphoglycerate kinase 594
 - phosphoglycerate phosphomutase 600
 - phosphopyruvate hydratase 600
 - phosphoric esters 563
- Plasma, phosphorus 563
- placental lactogen 721
 - plasmalogens 604
 - plasmin 410
 - PORTER-SILBER chromogens 745
 - potassium 564
 - potassium exchange 526
 - pregnanediol 753, 754
 - pregnanetriol 745
 - progesterone 753, 754
 - proteins 579 sq.
 - allotypy 634
 - in bile 655
 - calculation of ionized calcium from 565
 - cation concentration from specific conductivity and 562
 - conversion factors 276
 - in faeces 289, 659
 - in neoplastic disease 581
 - osmotic activity 526
 - in pregnancy and post partum 691
 - in semen 684
 - protein-bound iodine 564, 726
 - protein nitrogen 572
 - protein sulphur 563
 - protoporphyrin 576
 - unconjugated pterins 610
 - purines 577
 - pyridoxal phosphate 610
 - pyruvate kinase 594
 - pyruvic acid 607
 - renin 598, 741
 - riboflavin 471, 609
 - ribosephosphate isomerase 600
 - secretin 739
 - serotonin 575
 - salic acid 606
 - β_2 -siderophilin 583
 - sodium 565
 - sodium exchange 526
 - specific conductivity 560
 - cation concentration from protein content and 562
 - specific gravity 557
 - specific heat 560
 - sphingomyelin 604
 - succinate dehydrogenase 592
 - succinic acid 607
 - sulphate 553
 - 6-sulphatoxyskatole 575
 - sulphur 563
 - testosterone 732
 - thiamine 470, 609
 - thiocyanate 564
 - thyroid hormones 726, 727
 - thyrotropin 718
 - thyroxine 288, 726, 727
 - tocopherols 609
 - transcobalamins 484
 - triglycerides 601, 604
 - trihydroxycholic acid 601
 - tri-iodothyronine binding 726
 - triosephosphate isomerase 600
 - trypsin-inhibiting capacity 598
 - ubiquinone-50 609
 - urea 572
 - osmotic activity 526
 - glomerular filtration rate and 531, 532
 - uric acid 577
 - in gout 453
 - uronic acid 606
 - vasopressin 723
 - viscosity 558
 - vitamin A 457, 609
 - vitamin B₁ 475, 609
 - vitamin B₁₂ 484, 610
 - vitamin D 461, 609
 - vitamin E 466
 - volume 554 sq.
 - nomogram 556
 - tracer study 289
 - water 561
 - weight gain in pregnancy 690, 691
 - xanthine 577
 - xanthine oxidase 592
 - L-xylulose 567
 - zinc 621
- Plasmacytes in bone marrow 365, 376
- Plasmalogens 604
- in cerebrospinal fluid 634
 - in erythrocytes 604
 - in plasma 685
 - in spermatozoa 410, 622
- Plasmin 410, 622

[illegible]

- gain in pregnancy	690
- properties, isotopes, etc.	235
- protein formation	433, 435, 436
- in saliva	644
- in semen	683
- in skin	520
- in sweat	680
- in synovial fluid	641
- in teeth	521
- in thrombocytes	564
- in urine	663
Potassium-42, characteristics	292
- decay table	295
- gamma ray constant	231
Potassium acetate solutions, conversion factors	274 sq
- pH values	279
Potassium aluminium sulphate solutions, pH values	279
Potassium bicarbonate solutions, conversion factors	274 sq
- decinormal	277
- mEq ml ⁻¹	277
Pyrimine	69
Radiation	69
- decinormal	277
Potassium citrate solutions, conversion factors	274 sq
Potassium cyanide, decinormal solutions	277
Potassium dichromate, decinormal solutions	277
Potassium dihydrogen phosphate solutions, pH values	279
Potassium D-glucuronate solutions, conversion factors	274 sq
Potassium hydroxide, decinormal solutions	277
Potassium oxide, conversion factor into potassium solutions, conversion factors	274 sq
- decinormal	277
Potassium permanganate, decinormal solutions	277
Potassium phosphates, solutions, conversion factors	274 sq
- effect on urinary osmolality and specific gravity	534
Potassium sulphate, effect on urinary osmolality and specific gravity	534
Potassium tartrate, decinormal solutions	277
Potassium tetroxalate solutions, decinormal - pH values	279
Poisonous, amino acids	516
- composition	50
- vitamin losses during cooking	50
- sweet, composition	50
Formal difference, electric and magnetic field, composition	512 sq
Pound	20
- 'apothecaries'	20
- Troy	20
Poundst	20
Pound force	21
Powers	133, 13
Power units	21
Powering vector	21
Pr See Praxedodimium	
Praxedodimium, flame lines	28
- properties, isotopes, etc	28
Prealbumin, amino acid composition	58
- in cerebrospinal fluid	63
- characteristics and function	58
- in faeces	63
- thyroxine binding	72
Prodinsulose	36
- biological activity	75

androgens	751
ascorbic acid	611
caeruloplasmin	593
calcium	565
catechins	609
changes	691
cholesterol	601, 603
coagulation	622
copper	556
crassine kinase	594
enzyme activities	586
erythrocyte count	614
erythrocyte sedimentation rate	559
fatty acids	601, 603
folic acid	610
glucose	604
β -glucuronidase	597
glycerols	603
glycoproteins	606
haematocrit	614
haemoglobin	615
insulin	736
protein-bound iodine	564
iron	566
lactate	607
leucocyte count	618
lipids	601, 603
nonprotein nitrogen	572
oestrogens	755
phosphate	563
phosphatides	601, 603
phosphoethanolamine	573
placental lactogen	721
pregnanediol	753
proteins	583
trans-angiotensin	741
riboflavin	609
thiamine	609
tocopherols	620
urea	672
vitamin A	609
vitamin B ₁	609
vitamin B ₂	610
volume	555
zinc	567
BAR	339
calcium requirement	493, 494
erythrocyte sodium	740
erythropoiesis	745
folic acid deficiency	755
lactation production	753
salivary pH value	643
effects of sex hormones	758
thiamine requirement	727
thyroid hyperfunction	727
organic components of tissues	522
urine, amino acids	667
calcium	664
chorionic gonadotropin	715
cholesteroles	749
crenine	665
erythrocytes	677
fluoride	673
follicle stimulating hormone	663
lactose	677
leucocytes	673
melanotropin	677
3-methyl-2-pyridone 5-carboxylamide	722
oestrogens	756, 757
oestrogen metabolites	432
pregnanediol	754
pregnanolone	754
urea	665
urine, electrolyte sensitivity	723
vitamin A deficiency	665
vitamin B ₂ requirement	625

- Pregnancy (*contd.*), vitamin D 464
 – poisoning 464
 – requirement 461
 – weight gain 690
 Pregnane 381
 5 α -Pregnanediol. See α -Allopregnanediol
 5 β -Pregnanediol 380
 – in meconium 754
 – in plasma 753, 754
 – from progesterone 753
 – in urine 754
 5 α -Pregnane-3 α ,11 β ,17 α ,20 β ,21-pentol 379
 5 β -Pregnane-3 α ,11 β ,17 α ,20 α ,21-pentol 379
 5 β -Pregnane-3 α ,11 β ,17 α ,20 α ,21-pentol 379
 5 β -Pregnane-3 α ,11 β ,17 α ,20 β ,21-pentol 379
 Pregnanetriol 380
 – breakdown 746
 – in plasma 745
 – secretion 745
 – in urine 747
 5 β -Pregnane-3 α ,17 α ,20 α -triol. See Pregnanetriol
 Pregnanolone 380
 – from progesterone 753
 – in urine 754
 Pregn-4-ene-3,20-dione. See Progesterone
 Pregnenolone 380
 – biosynthesis 401, 428, 429
 – production rate 753
 Prekallikrein 742
 Premature infants, blood, amino acids 574
 – ammonia 573
 – aspartate aminotransferase 593
 – bilirubin 576
 – cations 561
 – fructosediphosphate aldolase 599
 – glucose 605
 – lactate dehydrogenase 590
 – blood pressure 553
 – cerebrospinal fluid, leucocyte count 635
 – protein 637
 – erythroblastosis 612
 – erythrocytes, lifetime 616
 – mean corpuscular haemoglobin 615
 – treatment of rickets 464
 – urinary concentration 662
 – urine, amino acids 666, 667
 – creatine 665
 – creatinine 665
 – proteins 668
 – volume 661
 – vitamin E deficiency 466
 – vitamin K therapy 468
 – weight gain 692
 Pressure, standard atmospheric 212
 – units 211
 – values, correction 255
 Pretzels, composition 508
 PRF (prolactin-releasing factor) 725
 Primquine sensitivity, enzymes in 592
 Prime numbers 9
 Pro. See L-Proline
 Probit transformation 54, 55, 163, 164
 Procaine benzylpenicillin, reference preparation 762
 Procarboxypeptidases in pancreatic juice 652
 Procarboxypeptidase A 409
 Pro-erythroblasts 612
 Pro-erythrocytes. See Reticulocytes
 Progestagens. See Progestational hormones
 Progestational hormones 379, 380, 753 sq.
 – accumulation 456
 Progesterone 380, 753 sq.
 – biological activity 754, 755, 758
 – biosynthesis 428, 429
 – effect on gonadotropin secretion 714
 – in plasma 753, 754
 – production rate 753
 Proinsulin 735
 Prolactin 718, 719
 – chorionic growth-hormone 721
 – standard 762
 Prolactin-inhibiting factor 719, 725
 Prolactin-releasing factor (PRF) 725
 Prolamines 329
 Prolidase 408, 410
 Prolinase 408, 410
 D-Proline degradation 395
 L-Proline (Pro) 332
 – in blood 449, 574
 – in blood proteins 581
 – degradation 394, 395, 402
 – in foods 516
 – formation 432
 L-Proline, hydroxylation, ascorbic acid in 490
 – in milk 688
 – in saliva 645
 – in sweat 680
 – in urine 449, 667
 Promethium, properties, isotopes, etc. 240
 Promyelocytes in bone marrow 621
 1,3-Propanediamine in semen 684
 Propanoic acid. See Propionic acid
 Propenoic acid 368
 Propentdyopents 364
 Propionaldehyde from α -methyl- β -alanine 401
 Propionic acid 366
 – in blood 607
 – in cholesterol degradation 401
 – in faeces 660
 – in valine degradation 396
 Propionic aldehyde in valine degradation 396
 Propionyleholine, hydrolysis 414
 Propionyl-CoA-carboxylase, biotin in 487
 Propionyl-coenzyme A, in α -aminobutyric acid degradation 396
 – in degradation of fats 392
 – in isoleucine degradation 396
 – in α -methyl- β -alanine degradation 401
 – in norleucine degradation 396
 – in L-threonine degradation 397
 – in valine degradation 396
 Propyl red indicator 283
 Prostaglandins 373, 492
 – in semen 685
 Prostate, carcinoma, serum acid phosphatase 596
 – 5'-nucleotidase 418
 – secretion 682 sq.
 – weight 710
 Prosthetic groups 382, 385
 Protactinium, properties, isotopes, etc. 246
 Protamine, reference preparation 763
 – sulphate, haemorrhagic diatheses and 623
 Proteases. See Proteolytic enzymes
 Proteins 329
 – in bile 655
 – biosynthesis 353, 354
 – in whole blood 579
 – in whole body, gain in pregnancy 690
 – in body fluids 523
 – in brain and spinal cord 520
 – calorific value and respiratory quotient for 539
 – in cerebrospinal fluid 637
 – conversion factors 523
 – dietary requirements 493 sq.
 – enzymes attacking. See Proteolytic enzymes
 – in erythrocytes 579
 – in faeces 659
 – in foods 498 sq.
 – in gastric juice 650
 – urinary concentration and 534
 – intake, blood urea and 572
 – in intestinal juice 656
 – ionized, buffer capacity in blood 527
 – in leucocytes 579
 – metabolism, effect of corticosteroids 749
 – effect of growth hormone 720
 – effect of oestrogens 757
 – effect of testosterone 752
 – water from 524
 – in milk 511, 688
 – nitrogen, in blood 572
 – conversion factors 251
 – in pancreatic juice 652
 – para-. See Paraproteins
 – in plasma. See Plasma proteins
 – in saliva 645
 – in semen 684
 – in serum (*ret. also Plasma proteins*) 579, 582
 – sulphur, in blood 563
 – in synovial fluid 641
 – in thrombocytes 579
 – in tissues 522
 – in urine 453, 668
 Protein-bound carbohydrates. See Glycoproteins
 Protein disulphide reductase, insulin degradation by 736
 Proteinuria in cystinosis 449
 Proteolipid protein in brain and spinal cord 520
 Proteolytic enzymes 405 sq.
 – in gastric juice 650
 – in pancreatic juice 652
 – precursors 406, 407
 Prothrombin 622
 – deficiency 449
 – vitamin K and 467, 468
 – thrombin from 410
 Prothrombin time 625
 Protocollagen 432
 Protohaem. See Haem
 Proton, charge: mass ratio 229
 – Compton wave length 229
 – gyromagnetic ratio 229
 – magnetic moment 229
 – mass 229
 – rest mass 229
 Protoporphyria, erythropoietic 455, 576
 Protoporphyrin 355, 358
 – in erythrocytes 455, 576
 – in faeces 659
 – in haem synthesis 454
 – in serum 576
 Protoporphyrinogen in haem synthesis 454
 Provitamins 461, 462
 Provitamin, animal. See 7-Dehydro-cholesterol
 Prunes, composition 501
 PS (metric horsepower) 214
 Pseudohyperparathyroidism 728
 Pseudouridine 354
 – in s-RNA 351
 – in urine 671
 Pseudovitamin B₁₂ 483
 Psicose (D-allulose) 311
 Psoriasis, uric acid excretion 671
 PSP (phenolsulphobonphthalein) test 532, 533
 pt (pint) 204
 Pt. See Platinum
 PteGlu₁ (pteroyltriglutamic acid) 480
 PteGlu₂ (pteroylheptaglutamic acid) 480
 Pteridines, folic acid synthesis from 478
 Pterins, unconjugated, in blood 610
 Pteroyltriglutamic acid. See Folic acid
 Pteroylheptaglutamic acid (PteGlu₂) 480
 Pteroyltriglutamic acid (PteGlu₁) 480
 Pyralin in saliva 645
 Pu (plutonium) 248
 Puberty, bone development and 706, 707
 – pseudo-precocious, and ossification 707
 Puerperium, urinary creatine 665
 Pulmonary circulation 543, 544
 – embolism, serum enzyme changes 587
 – resistance 546
 – in children, determination 549
 – values 552
 Pulsatane units 205
 Pumpkins, composition 505
 Purine 336
 Purines 338
 – biosynthesis 433 sq., 479
 – in blood 577
 – in faeces 659
 – in faeces 478
 – folic acid synthesis from 399 sq.
 – metabolism 453
 – inborn errors 671
 – in urine 401
 Purine deaminases 418
 Purine nucleoside phosphorylase 400, 401
 – in purine degradation 401
 Purine oxidases 455
 Purpura 505
 Purslane, composition 394
 Putrescine, formation from ornithine 684
 PVI. See Polyvinylpyrrolidone
 Pylonephritis, chronic, fluid deprivation test in 535
 Pyramidal, geometry 308
 Pyran 308 sq.
 Pyranoses 336
 Pyridine 477
 Pyridine-3-carboxylamide 473, 474
 Pyridine-3-carboxylic acid. See Nicotinic acid
 Pyridine nucleotides, in biological oxidations 402, 404
 – redox potential 403
 Pyridoxal 473, 474
 – phosphate 473, 474
 – in blood 610
 – in enzymatic reactions 475
 – in glycogen phosphorylase 411
 Pyridoxal kinase in vitamin B₆ interconversions 473, 475
 Pyridoxamine 473, 474
 – phosphate 475
 – in enzymatic reactions 475
 Pyridoxamine phosphate oxidase in vitamin B₆ interconversions 473
 Pyridoxic acid 473, 474
 – in blood 610
 – in urine 675

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198.

[illegible]

- Rheumatoid factor, serum viscosity and . . . 558
 Rh-Hr phenomena and genotypes . . . 629
 Rhizopterin . . . 480
 Rhodium, flame lines . . . 284
 - properties, isotopes, etc. . . . 238
 Rhodopsin . . . 457
 - in isomerization of retinal . . . 460
 Rhubarb, composition . . . 505
 Ribitol . . . 322
 Ribitol teichoic acids, formation . . . 349
 Riboflavin . . . 471 sq.
 - antagonists . . . 472
 - in blood . . . 471, 609
 - deficiency . . . 472
 - dietary requirements . . . 472, 493
 - in erythrocytes . . . 471, 473
 - in foods . . . 499 sq.
 - losses during cooking . . . 498
 - in leucocytes . . . 471
 - in milk . . . 689
 - 5'-phosphate. See Flavin mononucleotide
 - in tryptophan metabolism . . . 475
 - in urine . . . 471, 473, 676
 D-Ribofuranose. See D-Ribose
 Ribonuclease (RNAase) . . . 406, 418
 - in cerebrospinal fluid . . . 638
 - in gastric juice . . . 650
 - isozymes . . . 584
 - pancreatic, reactions catalysed by . . . 406
 - in pancreatic juice . . . 652
 - structure and synthesis . . . 382
 - in urine . . . 672
 Ribonucleic acid (RNA) . . . 351 sq.
 - amino-acid acceptor . . . 351
 - biosynthesis . . . 352
 - effect of testosterone . . . 753
 - enzymatic cleavage . . . 406
 - depolymerization . . . 418
 - in leucocytes . . . 578
 - messenger . . . 351, 353
 - formation, effect of corticosteroids . . . 749
 - ribosomal . . . 351
 - soluble . . . 351, 353
 - transfer . . . 351, 353
 - viral, synthesis . . . 352
 Ribonucleosides . . . 337
 Ribonucleotides . . . 337
 5'-Ribonucleotide phosphohydrolase. See 5'-Nucleotidase
 Ribonucleotide reductase, vitamin B₁₂ in . . . 485
 D-Ribose . . . 310, 314
 - in bile . . . 655
 - in saliva . . . 646
 D-Ribose 1,5-diphosphate . . . 318
 D-Ribose 1-phosphate . . . 317
 - formation from nucleosides . . . 339, 340
 - in purine degradation . . . 400
 D-Ribose 5-phosphate . . . 318
 - formation from glucose . . . 420
 - in inosinic acid formation . . . 433
 - in degradation of pentoses . . . 399
 - in pentose phosphate cycle . . . 421, 422
 Ribosephosphate isomerase, in cerebrospinal fluid . . . 638
 - in pentose phosphate cycle . . . 422
 - in plasma . . . 600
 D-Ribose-5-phosphate ketol-isomerase. See Ribosephosphate isomerase
 D-Ribose 5-phosphate-1-pyrophosphate . . . 318
 - in inosinic acid formation . . . 433
 - in pyrimidine synthesis . . . 439
 'Ribosides' . . . 337
 Ribosomes . . . 351, 353, 354
 Ribosyladenine. See Adenosine
 Ribosyladenine 5'-phosphate. See Adenosine monophosphate
 Ribosylamine 5'-phosphate . . . 342
 - biosynthesis . . . 453
 - in inosinic acid formation . . . 433
 Ribosyl-5-amino-4-carboximidazole 5'-phosphate in inosinic acid formation . . . 435
 1-Ribosyl-5-aminoimidazole-4-carboxamide 5'-phosphate . . . 342
 - in inosinic acid formation . . . 435
 1-Ribosyl-5-aminoimidazole 5'-phosphate . . . 342
 - in inosinic acid formation . . . 433, 435
 Ribosyl-5-amino-4-succinocarboxamidoimidazole 5'-phosphate in inosinic acid formation . . . 435
 Ribosylases . . . 337
 - phosphates . . . 337
 Ribosylcytosine. See Cytidine
 Ribosyl-5-formamido-4-carboxamidoimidazole 5'-phosphate in inosinic acid formation . . . 435
 Ribosylformylglycinamide 5'-phosphate . . . 342
 Ribosylformylglycinamide 5'-phosphate . . . 342
 - in inosinic acid formation . . . 433
 Ribosylglycinamide 5'-phosphate . . . 342
 - in inosinic acid formation . . . 433
 Ribosylguanine. See Guanosine
 Ribosylguanine . . . 354
 Orotidine monophosphate . . . 340
 Ribosyluracil . . . 340
 5-Ribosyluracil. See Pseudouridine
 Ribosyluric acid . . . 341
 Ribosylxanthine. See Xanthosine
 'Ribotides' . . . 337
 D-Ribulose . . . 311, 314
 - 5-phosphate . . . 318
 - in pentose phosphate cycle . . . 421, 422
 - in urine . . . 673
 Ribulosephosphate 3-epimerase in pentose phosphate cycle . . . 422
 Rice, amino acids . . . 516
 - composition . . . 508
 Ricinoleic acid . . . 372
 Rickets . . . 453, 461, 464
 - serum alkaline phosphatase . . . 596
 - vitamin D-resistant . . . 449, 452, 453
 Rifamycin SV, reference preparation . . . 762
 Right angle . . . 207, 208
 RINGER infusion solutions . . . 529
 Ristocetins, reference preparations . . . 762
 RMR (resting metabolic rate) . . . 495
 Rn (radon) . . . 244
 RNA. See Ribonucleic acid
 RNAase. See Ribonuclease
 RNA nucleotidyl transferase . . . 352, 353
 RNA polymerase . . . 352, 353
 ROBISON ester. See D-Glucose 6-phosphate
 ROBISON-TANKO ester. See D-Fructose 1-phosphate
 Rod (unit) . . . 200
 Rod vision quantities . . . 223
 Roentgen . . . 219
 Rolitetracycline, standard . . . 761
 Rood . . . 203
 Roots (arithmetic) . . . 132 sq.
 - square, tables . . . 20 sq.
 Rosolic acid indicator . . . 283
 Rotational frequency units . . . 208
 Rotor syndrome . . . 454
 - serum bilirubin . . . 577
 Round cells . . . 614
 Rous sarcoma, lactic acid fermentation . . . 388
 - respiratory rate . . . 387
 RQ (respiratory quotient) . . . 539
 RSH. See Coenzyme A
 Ru. See Ruthenium
 Rubella antiserum, reference preparation . . . 761
 Rubidium, in blood . . . 567
 - flame lines . . . 284
 - properties, isotopes, etc. . . . 237
 - in synovial fluid . . . 641
 Rubidium-86, characteristics . . . 292
 Rum, composition . . . 509
 Runs . . . 194, 195
 - tables . . . 129, 130
 Rutabagas, composition . . . 506
 Ruthenium, flame lines . . . 284
 - properties, isotopes, etc. . . . 238
 RV (residual volume of air in lungs) . . . 541, 542, 550, 551
 Ry (rydberg) . . . 213
 Rydberg . . . 213
 RYDBERG constants . . . 229
 Rye, amino acids . . . 516
 Rye bread, composition . . . 508
 Rye flour, composition . . . 508
 S
 σ (standard deviation) . . . 158
 σ^2 (variance) . . . 158
 s (scruple) . . . 205
 s (second) . . . 205
 s⁻¹ (reciprocal second) . . . 208, 213
 s (estimate of standard deviation) . . . 159
 s² (estimate of variance) . . . 159
 S. See Sulphur
 Saccharase in intestinal mucosa . . . 413
 - in sucrose intolerance . . . 451
 Saccharic acids . . . 312
 Saccharides . . . 308 sq.
 Saccharose. See Sucrose
 Safflower oil, composition . . . 510
 SAHLI percentages . . . 615
 Salami, composition . . . 514
 Salicylic acid solutions, pH values . . . 279
 Saliva . . . 643 sq.
 - amount . . . 525, 643
 - α -amylase . . . 411, 645, 646
 - corticosteroids in plasma and . . . 745
 - electrolytes . . . 525, 643 sq.
 - lipase . . . 414
 - lysozyme . . . 413, 645
 Salmon, composition . . . 515
 Salsify, composition . . . 506
 Salt, table, iodination . . . 497
 Salts . . . 270
 Salt-losing nephritis . . . 662, 663
 Samarium, flame lines . . . 284
 - properties, isotopes, etc. . . . 240
 Sarcoma, lactic acid fermentation . . . 388
 - respiratory rate . . . 387
 Sardines, composition . . . 515
 SART (Stepped Atomic Time) . . . 207
 Sauerkraut, composition . . . 506
 Sausages, composition . . . 513, 514
 sb (stilb) . . . 223
 Sb. See Antimony
 Sc. See Scandium
 Scallops, composition . . . 515
 Scandium, flame lines . . . 284
 - properties, isotopes, etc. . . . 235
 Scarlet fever streptococcus antitoxin, standard . . . 760
 SCHAFFRA enzyme units . . . 584
 SCHICK test toxin, standard . . . 759
 SCHILLING's haemogram . . . 620
 SCHILLING's test . . . 289, 435
 Scintigraphy, thyroid . . . 288, 289
 Scintillation counters . . . 286
 Sclerosis, multiple, cerebrospinal fluid γ -globulin . . . 637
 - γ -globulin . . . 223
 Scotopic vision quantities . . . 205
 Scruple . . . 205
 Scurvy . . . 490
 Scyllitol in urine . . . 673
 SDH (sorbitol dehydrogenase). See L-Iditol dehydrogenase
 Se. See Selenium
 Sea foods, composition . . . 514, 515
 9,10-Secocholesta-5,7,10(19)-trien-3 β -ol. See Vitamin D₃
 Seco-compounds . . . 381
 Second . . . 205 sq.
 - reciprocal . . . 208, 213
 - 207, 208
 Second (angle) . . . 651, 739
 Secretin . . . 631, 632
 Secretin test . . . 631
 Secretors of ABH substances . . . 580
 Sedimentation constants of plasma proteins . . . 558, 559
 Sedimentation rate, erythrocyte . . . 311, 316
 D-Sedoheptulose . . . 621
 - 1,7-diphosphate . . . 603
 - in erythrocytes . . . 321
 - 7-phosphate . . . 421, 422
 - in pentose phosphate cycle . . . 673
 - in urine . . . 673
 Sedoheptulose-7-phosphate: D-glyceraldehyde-3-phosphate glycolaldehydetransferase in plasma . . . 619, 620
 Segmented cells, in blood . . . 621
 - in bone marrow . . . 369, 377
 Selacholeic acid . . . 567
 Selenium, in blood . . . 497
 - dietary requirements . . . 688
 - in milk . . . 237
 - properties, isotopes, etc. . . . 202
 Selenium-75, characteristics . . . 299
 - decay table . . . 682 sq.
 Semen . . . 418
 - 5'-nucleotidase . . . 755
 - oestrogens . . . 451
 Semidehydroascorbic acid . . . 682 sq.
 Seminal vesicles, secretion . . . 710
 - weight . . . 682
 Seminose. See D-Mannose
 Semolina, composition . . . 508
 Sequential analysis charts . . . (inside back cover)
 Ser. See L-Serine
 L-Serine (Ser) . . . 532
 - in blood . . . 531
 - in blood proteins . . . 414
 - cell constituents from . . . 374
 - decarboxylation . . . 396, 397, 410
 - degradation . . . 396, 397, 410

Spring in Florida

in synthesis of purines and methionine...	479	Sm See Samarium	760	Sodium oxide, conversion factor into sodium ..	274 sq
in saliva	645	Smulplex antiserum, standard	760	- solutions, conversion factors	277
in sweat	680	- vaccine, reference preparation	759	- decinormal	277
in thyroid hormone formation	440	Sn See Tin		Sodium phosphates, solutions, conversion factors	274 sq
		Snails, composition	315	- decinormal	277
		Soaps	565	- pH values	279
				Sodium salicylate solutions, conversion factors	274 sq
serine hydroxymethyltransferase, in glycine formation...	432			Sodium sulphate solutions, conversion factors	274 sq
- vitamin B ₆ and	475			Sodium sulphide, decinormal solutions	277
s ₁ -Seromucoid. See α_1 -Glycoprotein, acid				Sodium tetraborate, decinormal solutions	277
serotonin, in blood	575			- decahydrate, See Borax	
- in cerebrospinal fluid	448			Sodium thiosulphate solutions, conversion factors	274 sq
- degradation	394, 441				
- formation	434				
- and haemorrhagic diseases	623, 624	- in electrolyte balance	525	- concentration, measures	271
- in pineal gland	730	- in erythrocytes	565	- temperature variation	251
- in thrombocytes	575	- exchangeable	518, 526	- decinormal, of reagents	277
- in urine	669	- in faeces	658	- dissociation	278, 279
Serum (see also Plasma), albumin-globulin ratio	582	- flame lines	284	- ideal and real	270
- α amino acids in plasma and	573	- in foods	499 sq	- infusion. See Infusion solutions	
- enzyme activities in plasma and	556	- in gastric juice	649	- isotonic. See Isotonic solutions	
- proteins	579, 582	- glomerular filtration and excretion	536	- osmotic properties	279, 271
- fractions	583	- in hair and nails	620	- viscosity	214
- specific gravity	557	- in histological preparation	656	Somatotropic hormone. See Growth hormone	
- sulfate ionization	559	- in milk	588	Somatotropin-releasing factor	720
- thionin	410	- in muscle	518	SOMMERFELD fine-structure constant	228
- viscosity	558	- in organs	519	SOMMERFELD fine-structure constant	228
Serum groups	634, 809	- in pancreatic juice	652	SOMMERFELD fine-structure constant	228
Serum water, electrolyte composition	523	- in placenta	522	SOMMERFELD fine-structure constant	228
SGOT (serum glutamate-oxaloacetate transaminase)	523	- in plasma	565	SOMMERFELD fine-structure constant	228
SGPT (serum glutamate-pyruvate transaminase)	523	- gain in pregnancy	690	SOMMERFELD fine-structure constant	228
Sh (short hundredweight)	205	- properties, isotopes, etc	234	SOMMERFELD fine-structure constant	228
Sheep's milk, composition	581	- in saliva	644	SOMMERFELD fine-structure constant	228
Shimadzu enzyme units	581	- in semen	620	SOMMERFELD fine-structure constant	228
Short ton	205	- in skin	588	SOMMERFELD fine-structure constant	228
Shoulder, secondary ossification centres	706, 708	- in sweat	659	SOMMERFELD fine-structure constant	228
- width during growth	693 sq	- in synovial fluid	641	SOMMERFELD fine-structure constant	228
Shrimps, composition	513	- in teeth	521	SOMMERFELD fine-structure constant	228
Sh in (short ton)	205	- in urine	663	SOMMERFELD fine-structure constant	228
Shunt volume, intrapulmonary	544	Sodium-22, characteristics	292	SOMMERFELD fine-structure constant	228
Sh. See Sulfon		- decay table	294	SOMMERFELD fine-structure constant	228
SI (International System of Units)	200 sq	- gamma ray constant	221	SOMMERFELD fine-structure constant	228
Silicic acids	311, 316	Sodium-24, specific activity	292	SOMMERFELD fine-structure constant	228
- effect on electrophoretic mobility of blood cells	560	- characteristics	292	SOMMERFELD fine-structure constant	228
- in brain and spinal cord	520	- decay table	294	SOMMERFELD fine-structure constant	228
- in cerebrospinal fluid	637	- gamma ray constant	221	SOMMERFELD fine-structure constant	228
- formation	423	Sodium acetate, buffer	280 sq	SOMMERFELD fine-structure constant	228
- in gangliosides	377	- solutions, conversion factors	274 sq	SOMMERFELD fine-structure constant	228
- in gastric juice	650	- pH values	279	SOMMERFELD fine-structure constant	228
- in plasma	606	Sodium ammoniosulphate, solutions, conversion factors	274 sq	SOMMERFELD fine-structure constant	228
- in saliva	645	Sodium benzoate solutions, pH values	279	SOMMERFELD fine-structure constant	228
- in semen	684	Sodium bicarbonate, solutions, conversion factors	274 sq	SOMMERFELD fine-structure constant	228
- in synovial fluid	642	- decinormal	277	SOMMERFELD fine-structure constant	228
- in urine	673	- for infusion	529	SOMMERFELD fine-structure constant	228
Silomucous, in gastric juice	650	- pH values	279	SOMMERFELD fine-structure constant	228
- in saliva	645	- effect on urinary osmolality and specific gravity	529	SOMMERFELD fine-structure constant	228
Silicic acid, enzyme units	584	Sodium bisulphate solutions, pH values	534	SOMMERFELD fine-structure constant	228
Sickle cells. See Erythrocytes, sickle cell		Sodium borate buffer	280 sq	SOMMERFELD fine-structure constant	228
Sickle cell anaemia. See under Anaemia		Sodium bromide solutions, conversion factors	274 sq	SOMMERFELD fine-structure constant	228
Sickle cell trait	448	Sodium carbonate, buffer	274 sq	SOMMERFELD fine-structure constant	228
Silicic acid	205	- solutions, decinormal	277	SOMMERFELD fine-structure constant	228
Silicic acid	205	- pH values		SOMMERFELD fine-structure constant	228

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198.

[illegible]

- L-Thyroxine (*contd.*), binding capacity of
 plasma for 726
 - biological activity 727
 - in blood 288, 726, 727
 - in cerebrospinal fluid 636
 - in faeces 727
 - in liver 727
 - metabolism 288
 - effect on thyrotropin secretion 718
 Thyroxine-binding globulin 726
 Ti. See Titanium
 Tick-borne encephalitis antisera, reference reagents 764
 Tidal volume, respiratory (V_T) 541, 550
 Tiglic acid 371
 Tiglyl-coenzyme A in isoleucine degradation 396
 TIM, See Triosephosphate isomerase
 Time units 205 sq.
 Timodonic acid 370
 Tin, in blood 567
 - in faeces 658
 - flame lines 284
 - properties, isotopes, etc. 238
 - in urine 664
 Tin-113, characteristics 293
 Tissues, active mass, and BMR 539
 - adipose, enzyme activities 585
 - effect of insulin 736
 - lactic acid fermentation 388
 - respiratory rate 387
 - buffer capacity 527
 - composition 517
 - enzymes 584 sq.
 - nonfatty, metabolic water 524
 - organic components 522
 - respiratory rates 387
 - soft, radiation absorption 220
 Tissue-specific enzymes 584
 Titanium, flame lines 284
 - properties, isotopes, etc. 235
 - in urine 664
 Tl. See Thallium
 TLC (total lung capacity) 542
 Tm. See Thulium
 Tm (renal function) 533 sq.
 Tocochromanol-3 465
 Tocol 465
 Tocols 465
 Tocopherols, See Vitamin E
 α -Tocopherol 465
 - in foods 499 sq.
 Tocopherol-like compounds 466
 Tocopheronic acid 466
 Tocopheronolactone 466
 α -Tocopherylquinone 466
 Tocotrienols 465
 Tolerance limits 150, 152, 154 sq.
 - tables 128
 Tomatoes, composition 506
 - losses during cooking 498
 - juice, composition 506
 - 205
 - 204
 - (in-force) 211
 - 211
 - composition 512, 513
 - 212
 - 760
 (triphosphopyridine nucleotide). See isotinamide-adenine dinucleotide
 phosphate
 See Thiamine pyrophosphate
 roy measure) 205
 isalolase in pentose phosphate cycle 421, 422
 isaminases 394
 - 655
 - 593, 594
 - 475
 isaminations, in amino-acid
 gradation 393, 397-399
 - 475
 iscarboxylation, biotin in 486, 487
 iscobalamins in serum 484
 iscortin 745
 iscription of DNA code 352, 353
 isferases 385, 386
 isferrin 289
 islotopy 634, 809
 isino-acid composition 581
 - 655
 - 580
 isaracteristics and function 580
 - 659
 - 645
 - 684
 Transferrin, in serum 580, 583
 - and serum iron 566
 - in urine 668
 Transferring enzyme in tricarboxylic acid
 cycle 390, 391
 Transfer RNA 351, 353
 α -Transformation 62, 64, 65, 180
 Transfusion, exchange, serum bilirubin as
 guide 577
 Transfusion reaction, haemolytic 632
 Transketolase, in pentose phosphate
 cycle 421, 422
 - in plasma 593
 Transketolase test in thiamine deficiency 470, 471
 Transmural pressure, vascular 544
 Transudates, electrolyte content 525
 Transuranic elements, properties and
 isotopes 248
 Trapczoid, geometry 142
 TRF (thyrotropin-releasing factor) 718, 725, 809
 Triacetyloleandomycin, reference preparation 762
 Triacetonole acid 367
 Triacylglycerols. See Triglycerides
 Triaminolone 380
 - biological activity 750
 Triangle, geometry 140, 141
 Tricarboxylic acid cycle 390, 391
 - and amino-acid degradation 393
 - in degradation of foods 402
 Trichinella antiserum, reference reagent 764
 Trichloroacetic acid solutions, pH values 279
 Tricosanoic acid 367
 Tridecanoic acid 366
 Tridecyllic acid 366
 Triene acids in serum lipids 604
 Trichanolamine buffer 280 sq.
 Triglycerides (see also *Fats*) 365, 374
 - accumulation 456
 - in bile 655
 - in cerebrospinal fluid 638
 - in erythrocytes 601
 - in faeces 659
 - formation 426
 - enzymatic hydrolysis 414
 - in plasma 601, 604
 - in spermatozoa 685
 - in synovial fluid 642
 Trigonelline in coffee 509
 Trigonometric functions 138, 139
 Trihydroxycholeic acid. See Cholic acid
 Trihydroxycoprostanic acid in bile 655
 3 α ,11 β ,21-Trihydroxy-20-oxo-5 β -pregnan-
 18-al 380
 11 β ,17 α ,21-Trihydroxypregna-14-diene-
 3,20-dione. See Prednisolone
 3 α ,17 α ,21-Trihydroxy-5 β -pregnane-11,20-
 dione 380
 3 α ,11 β ,21-Trihydroxy-5 β -pregnan-20-one 380
 3 α ,17 α ,21-Trihydroxy-5 β -pregnan-20-one 380
 11 β ,17 α ,21-Trihydroxypregn-4-ene-3,20-
 dione. See Cortisol
 9 α ,11 α ,15-Trihydroxyprosta-5,13-dienoic
 acid 373
 9 α ,11 α ,15-Trihydroxyprosta-5,13,17-trienoic
 acid 373
 9 α ,11 α ,15-Trihydroxyprost-13-enoic acid 373
 2,6,8-Trihydroxypurine. See Uric acid
 n-3,5,3'-Tri-iodothyronine, biological
 activity 727
 L-3,5,3'-Tri-iodothyronine (T_3) 333, 726
 - biological activity 727
 - in liver 727
 - plasma binding 726
 - test for thyroid function 288
 Triketohydrindene 329
 - hydrate. See Ninhydrin
 4,4,14 α -Trimethylcholesta-8,24-dien-3 β -ol.
 See Lanosterol
 4,4,14 α -Trimethyl-5 α -cholestane in steroids 381
 7,8,10-Trimethylisoxaloxazine 472
 (+)-2,4,6-Trimethyltetraacetic-2-enoic acid 372
 5,7,8-Trimethyltolcol. See α -Tocopherol
 5,7,8-Trimethyltocotrienol 465
 Triokinase in lactic acid fermentation 390
 Trioses 308, 313
 Triosephosphate in erythrocytes 605
 Triosephosphate dehydrogenase. See
 Glyceraldehydephosphate dehydrogenase
 Triosephosphate isomerase (TIM), in
 glucose 6-phosphate formation from
 glyceraldehyde 3-phosphate 422
 - in glycolysis 389
 - in plasma 600
 Triparanol and cholesterol synthesis 426
 Tripe, composition 512
 Tripeptides, enzymatic hydrolysis 499
 Triphosphopyridine nucleotide. See Nicotin-
 amide-adenine dinucleotide phosphate
 Triphosphoric monoester hydrolases 386
 Triple point of water 208, 209
 Trisaccharides as lipid component 365
 Tris buffer 280 sq.
 Trismaleate buffer 280 sq.
 Tritium, characteristics 234, 292
 t-RNA (transfer RNA) 351, 353
 Tropacolin indicators 283
 Tropical year 206
 Troposphere, composition 234 sq.
 Trout, composition 515
 Troy units 204, 205
 Trp. See L-Tryptophan
 Trunk, surface area 525
 Trypsin 407
 - in faeces 659
 - inhibition, in pancreatic juice 652
 - in serum 598
 - in pancreatic juice 653
 Trypsinogen 407
 - in pancreatic juice 652
 Tryptamine, in blood 575
 - in urine 669
 L-Tryptophan (Trp) 333
 - delayed absorption 452
 - in blood 574
 - in blood proteins 581
 - cell constituents from 434
 - dietary requirements 496
 - in foods 516
 - hydroxylation, dchydroascorbic acid and 490
 - 5-hydroxytryptamine from 441
 - loading test 665
 - metabolism 398, 399, 402
 - B vitamins in 473
 - metabolites in urine 668
 - in milk 688
 - nicotinic acid from 476, 477
 - in saliva 645
 - in sweat, enzyme changes 680
 - in urine 667
 Tryptophan oxygenase, effect of cortico-
 steroids 749
 TSG (thyroid-stimulating globulin) 718
 TSH (thyroid-stimulating hormone). See
 Thyrotropin
 TSH-RF (thyroid-stimulating-hormone
 releasing factor) 718, 725
 Tsuzic acid 368
 Tsubic acid 371, 372
 Tubercle bacilli, lipids 759
 Tuberculin, standards 759
 Tuberculostearic acid 371
 Tubules, transport functions 534, 535
 - inborn defects 452
 - effect of oxytocin and vasopressin 723, 724
 Tumours, blood, enzyme changes 557, 558
 - glyceraldehydephosphate dehydrogenase 592
 - pyruvate kinase 594
 - bone, leucocyte mobility 560
 - carcinoil, blood histamine 575
 - blood tryptamine 575
 - 5-hydroxyindoleacetic acid excretion 669
 - plasma kinins 742
 - thrombocyte serotonin 575
 Tungsten, properties, isotopes, etc. 515
 Tunny, composition 514
 Turkey, composition 506
 Turnips, composition 762
 Tylosin, standard 761
 Typhoid antiserum, reference preparation 759
 - vaccine, reference preparation 759
 Tyr. See Tyrosine
 Tyramine, formation from tyrosine 394
 - in urine 668
 Tyrosinaemia, familial 449
 Tyrosinase. See o-Diphenol oxidase
 Tyrosine (Tyr) 333
 - adrenaline and noradrenaline from 440
 - in blood 449, 574
 - in blood proteins 581
 - cell constituents from 434
 - decarboxylation 374
 - degradation 398, 402
 - in foods 516
 - melanin from 440
 - in milk 688
 - peptide-linked, in thyroid hormone
 formation 440
 - from phenylalanine 378, 430
 - in saliva 645

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198.

[illegible]

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- Urine (*contd.*), ketone bodies 674
 - ketopentoses 673
 - kynurenic acid 669
 - kynurenine 669
 - lactic acid 674
 - lactose 451, 673
 - lead 664
 - leucine 667
 - leucocytes 677
 - lipids 675
 - lysine 667
 - magnesium 664
 - malic acid 674
 - manganese 664
 - maple syrup 448, 449
 - melanin 661
 - melanotropins 722
 - mercaptans 663
 - mercury 664
 - metanephrine 668
 - methionine 667
 - 3-methoxy-4-hydroxymandelic acid 675, 733
 - 3-methoxy-4-hydroxyphenylacetic acid 675
 - 3-methoxy-4-hydroxyphenylglycol 675
 - 5-methoxytryptamine 669
 - α -methyl- β -alanine 401
 - methylamine 668
 - methylguanidine 666
 - 1-methylguanline 671
 - 1-methylhistidine 667
 - 3-methylhistidine 667
 - 1-methylhypoxanthine 671
 - 1,4-methylimidazoleacetic acid 670
 - methylmalonic acid 449, 674
 - 1-methylnicotinamide 477, 676
 - 1-methyl-2-pyridone-5-carboxylamide 477, 676
 - 5-methyltetrahydrofolic acid 479
 - molybdenum 664
 - mucopolysaccharides 668
 - myoglobin 671
 - nicotinic acid 477, 676
 - nitrate 664
 - nitrite 664
 - nitrogen 665
 - - contribution to BMR 539
 - nitrogenous substances 665 sq.
 - non-nitrogenous metabolites 674, 675
 - noradrenaline 668, 733
 - normetanephrine 668
 - odour 661
 - oestradiol-17 β 430
 - oestriol 430
 - oestrogens and metabolites 756
 - oestrone 430
 - organic acids 674
 - ornithine 667
 - orotic acid 453, 671
 - osmolality 533 sq., 662
 - oxalic acid 674
 - pantothenic acid 488, 676
 - parathyroid hormone 728
 - peptides 666
 - pH value 536, 662
 - phenol 675
 - phenols 675
 - phenylacetylglutamine 666
 - phenylalanine 667
 - phenylpyruvic acid 448
 - phosphate 663
 - phospholipids 675
 - phosphorus 663
 - physical properties 661, 662
 - piperidine 668
 - placental lactogen 721
 - porphobilinogen 670
 - porphyrins 357, 358, 454, 455, 661, 670
 - potassium 663
 - pregnancy. See under Pregnancy
 - pregnanediol 754
 - pregnanolone 754
 - pregnenolone 753
 - progesterone 753
 - progesterone metabolites 753, 754
 - proline 449, 667
 - proteins 668
 - purines 671
 - pyridoxic acid 676
 - pyrimidines 671
 - pyrocatechol 675
 - pyrophosphate 663
 - pyruvic acid 674
 - reducing substances 673
 - riboflavin 471, 473, 676
 - 5-ribosyluracil 671
 Urine, sediments 677, 678
 - serine 667
 - serotonin 669
 - sialic acid 673
 - silicate 664
 - sodium 663
 - solutes, caloric turnover and 534
 - - protein intake and 534
 - specific gravity 661
 - - osmolality and 534, 535
 - steroid hormones 430
 - succinic acid 674
 - sucrose 673
 - 'sugar' 673
 - sulphate 663
 - 6-sulphatoxyskatole 669
 - sulphur 663
 - sulphur amino acids 663
 - surface tension 661
 - taurine 667
 - testosterone 752
 - thiamine 470, 471, 676
 - thiocyanate 663
 - threonine 667
 - trace elements 664
 - tryptamine 669
 - tryptophan 667
 - tryptophan metabolites 668
 - turbidity 661
 - tyramine 668
 - tyrosine 449, 667
 - urea 665
 - uric acid 665, 671
 - urobilinogen 661, 670
 - urocanic acid 670
 - uromucoids 668
 - uropepsinogen 672
 - uroporphyrin 670
 - valine 667
 - vanillic acid 675
 - vasopressin 723
 - viscosity 661
 - vitamins 676
 - vitamin B₁ 676
 - vitamin B₂ 676
 - volatile acids 674
 - volume 661
 - - osmolality and 535
 - water turnover 524
 - xanthine 671
 - xanthurenic acid 669
 - xylose 673
 - L-xylulose 451
 - zinc 664
 Uroaldosterone 380
 Urobilins 362
 (+)-Urobilin 364
 Urobilin IX- α 364
 Urobilinogen, in faeces 659
 - in urine 661, 670
 (+)-Urobilinogen 362, 364
 Urobilinogen IX- α 362, 363
 Urocanic acid, in L-histidine degradation 395
 - in sweat 680
 - in urine 670
 Urocortisol 380
 Urocortisone 380
 Urokinase, reference preparation 763
 Uromucoids in urine 668
 Uronic acids 312, 323
 - degradation 401
 - in plasma 606
 Uropepsinogen in urine 672
 Uroporphyrins 355, 357
 - in erythrocytes 576
 - in urine 670
 Uroporphyrin I, accumulation 454
 - synthesis 454
 Uroporphyrin III in haem synthesis 454
 Uroporphyrinogens 356
 Uroporphyrinogen I, synthesis 454
 Uroporphyrinogen III in haem synthesis 454
 Uroporphyrinogen isomerase in
 erythropoietic porphyria 454
 Ursodeoxycholic acid in bile 655
 UT (Universal Time) 205 sq.
 UTC (Coordinated Universal Time) 207
 Uteroverdin 363
 Uterus, enzyme activities 585
 - effect of oestrogens 757, 758
 - organic components 522
 - effect of oxytocin and vasopressin 723, 724
 - effect of plasma kinins 742
 - effect of progesterone 754, 758
 Uterus, proteolytic enzymes 410
 - weight 710
 - - gain in pregnancy 690
 UTP. See Uridine triphosphate
- V
- V. See Vanadium
 V (volt) 215, 216
 V_A (alveolar ventilation) 542
 V_T (minute ventilation) 542, 550
 V_T (tidal volume) 541, 550
cis-Vaccenic acid 369
trans-Vaccenic acid 369
 Vaccines, standards and reference
 preparations for 759
 Vaginal secretion, β -glucuronidase 597
 - phosphogluconate dehydrogenase 591
 Val. See L-Valine
 Valency of elements 234 sq.
 L-Valeric acid 366
 - in faeces 660
 Valeryl-coenzyme A in norleucine
 degradation 396
 L-Valine (Val) 333
 - in blood 449, 574
 - in blood proteins 581
 - in cerebrospinal fluid 449
 - degradation 395, 396, 402
 - dietary requirements 496
 - in foods 516
 - in milk 688
 - in saliva 645
 - in sweat 680
 - in urine 667
 Vanadium, dietary requirements 497
 - properties, isotopes, etc. 235
 - in urine 664
 Vancomycin, standard 761
 VAN DEN BERGH reaction 576
 VAN DYKE protein 723
 Vanillic acid, from catecholamine breakdown 732
 - in urine 675
 VAN SLIKE's determination of amino acids 329
 Variance 158
 Vascular driving and transmural pressures 544
 - resistance 544
 Vasopressin 722 sq.
 - standard 762
 - and urinary concentration 533
 VC. See Vital capacity
 Veal, composition 514
 Vegetables, amino acids 516
 - composition 502 sq.
 - vitamin losses during cooking 498
 Vegetable fat, composition 374
 - oils, fatty acids 210
 Velocity, angular, units 228
 - of light 210
 - linear, units 514
 Venison, composition 560
 Venous blood, pH value 558
 - viscosity 554
 - volume 554
 Venous blood pressure 542, 543, 550
 Ventilation (respiratory) 542, 543, 550
 - function tests 543
 - maximum voluntary (MVV) 548
 - - determination from respiratory rate 544
 Ventilation/perfusion ratio 544
 Ventricular fluid. See Cerebrospinal fluid
 Verdoglobin in blood 360, 362
 Verdoglobin A 361
 Verdoglobin S 360, 362
 Verdohaemoglobin 761
 Viomycin, reference preparation 352
 Viral DNA and RNA, synthesis 214
 Viscosity units 547
 Vision, colour, plates for testing (inside back cover)
 Visual acuity, plate for testing (inside back cover)
 - pigments, vitamin A and 547
 Vital capacity (VC) 541, 542
 - nomograms 550, 551
 - values 609 sq.
 Vitamins 457 sq.
 - in blood 639
 - in cerebrospinal fluid 493, 494
 - dietary requirements 496
 - in faeces 458 sq.
 - in foods 493
 - - losses during cooking 650
 - in gastric juice 659
 - in milk 659

Index

2. Inserting name in the numerical tables (pages 25-331) and chapter on Statistical Methods (pages 145-190) will be found on pages 14*-145*

[illegible][illegible][illegible]

A detailed index to the statistical tables (pages 28-131) and chapter on Statistical Methods (pages 146-196) will be found on pages 197-198

- | | | | | | |
|-------------------------------------------|-----|--------------------------------------------|-----|------------------------------------------|-----------------|
| Zinc (<i>contd.</i>), flame lines | 284 | Zinc, in sweat | 680 | Zr (zirconium) | 237 |
| - freezing point | 209 | - in synovial fluid | 641 | z-transformation | 62, 64, 65, 169 |
| - in leucocytes | 567 | - in urine | 664 | Zwieback, composition | 508 |
| - in milk | 688 | Zinc-65, characteristics | 292 | Zwischenferment. See Glucose-6-phosphate | |
| - in organs | 519 | - decay table | 299 | dehydrogenase | 329 |
| - in pancreatic juice | 652 | Zirconium, properties, isotopes, etc. | 237 | Zwitterions | 329 |
| - in placenta and amniotic fluid | 522 | Zn. See Zinc | | Zymohexase. See Fructosediphosphate | |
| - properties, isotopes, etc. | 236 | ZOLLINGER-ELLISON syndrome, gastric | | aldolase | 426, 427 |
| - activation of proteases | 410 | acidity | 648 | | |
| - in semen | 683 | - gastric juice secretion | 647 | | |
| - sulphate, decinormal solutions | 277 | - gastrin | 739 | | |